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PREFACE.

IN preparing this compend the practical needs of the student have been considered, controversial matter and references to authors and articles have therefore been omitted, and the effort to simplify the subject steadily maintained. The chief text-books in English, French and German have been consulted, as well as many monographs and special articles, and it is believed that nothing included will be found at variance with the text-books used in American medical colleges.

Chapter VI. is based almost wholly upon a syllabus prepared by Prof. Jas. Ewing, of Cornell Medical College, for one of his classes, and my thanks are due him for permission to use it. I am indebted also to Dr. J. C. Johnston, of the same institution, for valuable hints and for the photographs which illustrate the chapter on neoplasms. The negatives for these and for Figs. 58, 77 and 78 were made by Dr. B. H. Buxton, of Cornell, and kindly loaned by him.

The facts of pathology are common property, and the desire to aid the student should characterize every teacher and author; my hope in issuing this and the companion volume is that the facts have been so presented as to accomplish the object cited.

A. E. T.

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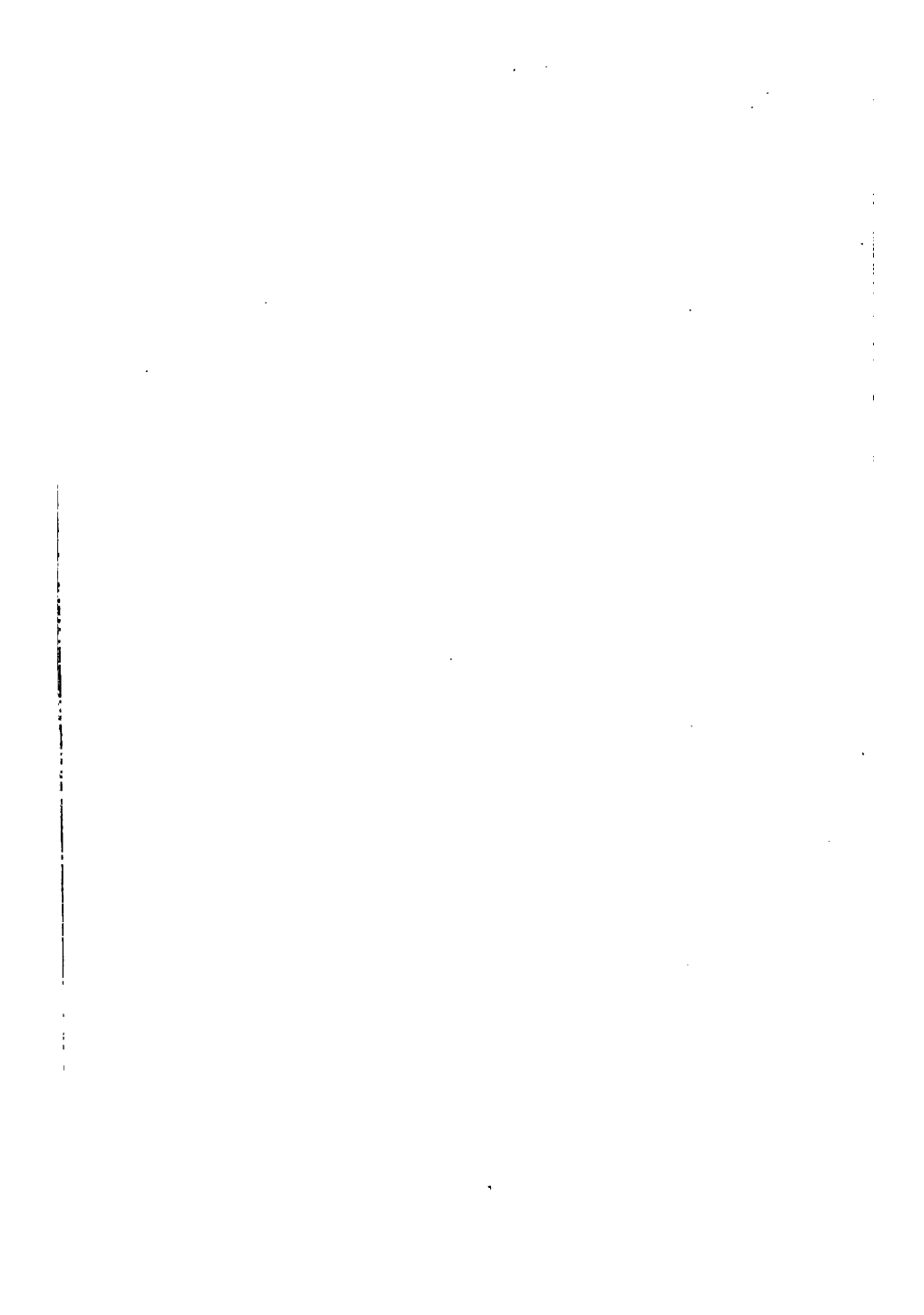


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ERRATA.

Page 42, line 7, for "fibromatous" read "fibrous."

" 181, line 11, for "work" read "growth."

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COMPEND OF PATHOLOGY.

PART I. GENERAL PATHOLOGY.

CHAPTER I.

DISEASE IN GENERAL ; ETIOLOGY.

Pathology is the science which treats of diseases, their causes, nature, signs, process, structural changes and results, and may be broadly divided into Plant and Animal Pathology ; the latter comprises Human Pathology, the subject of this work, and Animal Pathology which is a similar study of disease in animals. When the results of Animal and Human Pathology are studied as mutually interpretive it is called Comparative Pathology, a field still almost undeveloped. Some of the subdivisions of Pathology are so important to the physician that they are treated as separate branches, under the head of Symptomatology, Diagnosis, etc.; but strictly these belong to Pathology and they are easy to comprehend in proportion as one is familiar with Pathology in the narrow sense.

Human Pathology is divided into General and Special, the former considering processes or their results common to all or many forms of disease, and the latter such as are found in any one disease ; thus inflammation affects many different organs and diseases and belongs in General Pathology, while syringomyelia belongs only in a special organ, the spinal cord, and that special

affection of it. Further subdivisions of Pathology are Gross, treating of the naked-eye appearances of diseased organs and the technique of postmortem examinations ; Microscopic, the study of such organs by the microscope and the technique implied in such study ; Clinical, the examination of blood and discharges for the purpose of clinical diagnosis ; Morbid Function, called also Pathological Physiology ; Pathochemistry, etc.

Disease is that condition of an organism in which there is any departure from the normal in function, structure or relation ; it may be local or general, and tends to recovery or death.

Death is that condition of an organism in which further metabolism is impossible. It may be local or general and if local is called by the special names, gangrene, necrosis, caries, etc. This definition excludes cases of suspended animation or function, for in the proper conditions metabolism is still possible ; thus a portion of the organism may be frozen and apparently dead, and yet recover.

Etiology is the branch of pathology which considers the causes of disease. These may be *predisposing* or *exciting*, diminishing the resistance to disease or actually beginning it. *Predisposing causes* often become exciting by their relative severity. Among the common predisposing causes may be mentioned defective nourishment in utero ; premature birth and consequent feebleness from the start ; deficient food, oxygen and pure water ; bad sanitary conditions ; extreme changes in heat and atmospheric pressure ; great humidity especially with extreme temperature ; heredity, whose importance is less than has been taught formerly ; bodily and mental fatigue, starvation (up to the loss of about 33 per cent. of body weight), excessive bodily discharges, as of sweat and urine—any of these, alone or in combination, may predispose to disease, or beyond a certain degree actually excite it. *Exciting causes* are frequently injuries, extreme heat or cold suddenly applied, poisons developed in the body or taken in from without, parasites, including microorganisms. Certain diseases are almost wholly mechanical, as when valve defects in

the heart produce chronic passive hyperemia in the liver; others are especially chemical in their nature, as seen in bacterial invasions and consequent toxemia. More than one disease may exist in the same patient, and at times it is apparent that one is primary and the others are secondary;—thus inflammation of the lung spreads to the pleura, malignant disease of the stomach sets up similar changes in the liver, or obstacles in the lesser circulation cause passive hyperemia of the central veins of the liver with pressure atrophy of the hepatic cells, or a stone in the pelvis of the kidney descends and becomes a vesical calculus, or failure of the kidneys to eliminate urea, etc., causes colitis through the effort of the solitary glands in the colon to assume the duty.

Injuries may act suddenly, as in the case of blows or stabs; or slowly by lessening the space an organ ought to occupy, as when pleural exudate crowds a lung into a condition of atelectasis; or as a repetition of slight mechanical attritions, as seen in various trades where the use of a tool causes excessive development of the local epidermis. The results of injury are called contusion, wound, fracture, concussion, etc., and their usual common feature is tissue destruction and nerve irritation, with consequent disorder of circulation, inflammation, and growth changes.

Effects of heat and cold are strictly injuries but are usually considered by themselves. *Local excess of heat* causes relaxation of vessels, exudation of serum and blood, and finally charring, the effect depending on intensity and duration of cause; hyperemia, vesiculation, charring, and complete destruction being the so-called surgical degrees of burns; this grouping neglects the constitutional effects which are important according to the amount of tissue burned, a burn of one-third of the body surface usually causing death. The fatal result is explained by loss of function of skin, nervous shock, destruction of blood cells and plasma, toxic substances formed in the blood or absorbed from the burned surface, secondary intense internal congestion especially of the alimentary mucous membrane and perhaps embolism from

small vessels thrombosed by the heat. General excessively high temperature causes heat stroke, insolation, or heat exhaustion, with increased respiration and pulse rate, sweating, cerebral hyperemia and edema, and death from the latter or from albuminous coagulation throughout the body.

Extreme cold has somewhat similar effects leading to local or general death if severe and prolonged. Applied for a short time cold produces reflex vasomotor disturbances recognized under the popular term "catching cold." Either extreme of temperature is worse if associated with moisture.

Barometric pressure if diminished, as in mountain and balloon ascensions, or increased as in diving and caissons, may cause bleedings, drowsiness, ataxic gait, vomiting, delirium and even various paralyses.

Electric currents, either as lightning stroke, or from a dynamo, may cause burns of the integument, often curiously distributed over the surface, and injuries to the nervous system or to other organs.

Poisons.—Any substance which when introduced into the body in relatively small amount will cause injury or death otherwise than mechanically is called a poison, and may be either vegetable, mineral, or gaseous in origin. Grouped according to their action in the organism poisons are :

Irritants, including pure irritants, not chemically destructive, as arsenic ; corrosives, destroying tissue, as mineral acids ; and neurotics acting on the nervous system.

The latter include simple narcotics, as opium ; acro-narcotics, with strong irritating action, as aconite and strychnine ; septics, derived from albuminous decay and acting through destruction of the blood.

Auto-intoxication.—It is a law that any organism is self-destructive if compelled to reabsorb the waste products of its own

metabolism, and to this the human being is no exception. He may poison himself by means of any of his excreta, and to the special form of this which is due to putrefaction within the alimentary canal the name auto-intoxication has been given; this and allied forms will be treated in Chaps. IV.-V., while the effects of introduced poisons will be considered in Part II., Chap. XI.

Various circumstances affect the action of poisons of either of the classes cited above. Thus, a poison like carbolic acid, if introduced in concentrated form into the empty stomach, may cause death instantaneously by shock, or secondarily by its action on the alimentary mucous membrane, while, if dilute before ingestion or mixed with stomach contents, there may be time for absorption and general effects as well as the local reaction. In the one case the esophagus and fundus of the stomach may be the seat of its action, in the other the acid may ride over the stomach contents and affect the pylorus or the duodenum alone. Again, a patient who has been taking a drug and thus acquired a tolerance for it may resist a dose which would prove fatal in another. Too large a dose may cause vomiting and prevent a fatal result, while less may cause death at once or after an appreciable interval. Many poisons, if given in small amounts, may set up secondary tissue changes, which mask the action of the poison and hence are fatal indirectly, as in chronic arsenic and mercurial poisoning.

The action of poisons in general may impair the blood in its cells or plasma, or modify the organs, or inhibit function without producing gross anatomical change.

Blood Poisons.—The *blood poisons* are either liquid and volatile or gaseous, or they may be solid matters held in suspension by tissue juices and absorbed from wounds or the intestine or introduced directly into the blood-channels. They may prevent the exchange of gases in the blood by making a combination with the hemoglobin which is stronger than that with atmospheric oxygen, of which the standard and commonest is carbon

monoxide (illuminating gas poisoning), death then being due to an asphyxia generalized throughout the tissues ; or they may alter the hemoglobin after the red cells are affected, as is seen in the cyanosis following the administration of many coal-tar derivatives ; or they may cause tissue changes in addition, as in the case of ricin (from *Ricinus communis*) ; or they may affect the plasma, increasing its tendency to coagulate and thus producing thrombosis, as is the case with albumose, carbon dioxide, and a few others.

Corrosive Poisons.—*Poisons which cause tissue changes* as their chief effect usually attack the parts with which they are in contact, as the alimentary mucous membrane and the skin. The typical examples of this action are furnished by the acids and alkalies, which abstract water from the part, coagulate its albumins, form soapy or gelatinous compounds with its elements, etc. Frequently there is a pronounced and characteristic alteration in the color of the part, as in the yellow of nitric acid poisoning and the black of sulphuric. All degrees of effect may be found from simple redness or inflammation to necrosis and sloughing. Such poisons are usually called caustic or corrosive. A special case of the corrosive poisons is found in the irritant gases and volatile compounds which attack the conjunctiva and the respiratory mucous membrane ; examples are ammonia, formaldehyde, chlorine and bromine. These may cause edema or inflammation of the parts mentioned. Other poisons of this class act both locally and at a distance, like carbolic acid which causes a white eschar of the stomach mucous membrane with rigidity of the rugæ, and also acute inflammation of the organs which excrete it, the kidneys. Mercury bichloride, cantharidin, and to a certain extent phosphorus and arsenic also belong in this group.

Nerve Poisons.—Among the poisons which cause death without appreciable tissue change, hence called heart or nerve poisons, may be mentioned alcohol, amanita muscaria, strychnine, atropine and many other alkaloids. In large doses they act immediately upon the centers for respiration and circula-

tion, or the cord, or the cardiac muscle and ganglia, and are rapidly fatal; in smaller and frequent doses they may cause degeneration in the nervous tissues and consequent paralysis.

Disease caused by parasites, and by that special division of these known as microörganisms, will be treated in Chapters VIII. and IX.

Foreign Bodies.—A further cause of disease may be found in the introduction of lifeless foreign bodies into the organism, good examples of which are fatty embolism of the capillaries after fractures, air in the veins, foreign bodies in the larynx and trachea, all of which mechanically interfere with the function of lungs or heart; bits of catheters or other substances in the bladder which may form the nuclei of large calculi; beside their mechanical effects such foreign bodies may irritate the tissues and cause inflammation or deprive a part of its nutrition and cause atrophy.

Though one or more of the causes mentioned may excite disease, yet the peculiar results of such action vary within wide limits, being modified as to time (acute, subacute and chronic disease), by the age and condition and sex of the patient, by previous or intercurrent attacks of another nature, by tendencies to rhythmic cycles in the disease itself and many other and more obscure influences.

CHAPTER II.

DISORDERS OF DEVELOPMENT; TERATOLOGY.

UPON the developing embryo we may suppose that two sets of influences are acting, which we must be content to name without understanding. The first is the innate self-developing power of the embryo, and the other is complex, derived from the maternal structures as uterus, blood and nerves, and to an extent, increasing with growth, from the outside world. In proportion as the balance between these influences is disturbed the fetal parts are imperfectly developed, making malformations if slight and monsters if more pronounced; a fairly accurate distinction between them being that the malformation may be produced late in fetal life and not be incompatible with extra-uterine existence, while the monstrosity usually results from very early interference with the growth process and if marked renders the child non-viable.

Congenital Abnormality.—Congenital departures from the normal are usually divided into the single and double anomalies and may result from internal or external causes. As due to internal causes we consider all variations from the type, which if persistent would tend to make new species, and partly explain them by assuming some abnormality in either the male or the female element, or some incompatibility between them, perhaps essentially a question of physiological chemistry; when the variation appears in parent and child we speak of inherited abnormalities, as seen in the frequent occurrence of extra teeth and digits in immediately succeeding generations, and the prevalence of certain diseases in a family where we suppose the existence of some bodily peculiarity to account for it;

if the abnormality skip a generation or two we speak of its later appearance as atavism.

External causes of variation, that is, external to the developing embryo, may be injury to maternal or fetal tissues, from jarring or pressure, disordered supply of nutrition (including oxygen), powerful nervous influences from the mother, and the actual transmission of disease from her to the child.

When the variation occurs in different cases with about the same characteristics we speak of it as *typical*; an instance of which would be harelip and club-foot; where it is entirely anomalous we call it *atypical*. The former are usually to be referred to internal and the latter to external causes.

Varieties of Congenital Malformation.—Among the single forms of congenital abnormality may be mentioned those due to

1. Defective or arrested growth, hypoplasia or aplasia: Example, dwarfing, absent limb or brain or small size in either; non-closure of parts, often in the middle line, causing clefts; adhesion of adjacent parts, as horseshoe kidneys.
2. Excess of growth and development; as giant size of a part, extra breasts, digits, hair, etc.
3. Wrong disposition of parts; dextrocardia.
4. Tissues in the wrong place, or fetal tissues persistent; causing heterotopous and heterochronous growths. (See Tumors, Chap. VII.)
5. Sex anomalies, true and false hermaphroditism. The embryo, potentially bisexual, normally develops one set of organs to the disadvantage of the other; variation here implies marked development of the subsidiary set of organs, which is common in slight degrees, to complete formation of both, true hermaphroditism, which is so rare that its existence has been denied.

Monstrosity.—True monstrosity is more common in the double forms and may appear as duplication of any part of the fetus or complete doubling, the twins being closely connected at some part; they are always of the same sex, usually joined at corresponding parts, as head, thorax or sacrum, and may be of

equal size or of all degrees of inequality. In one sense twin and triple births of separate children are abnormal, being reversions from the typical human single birth to the lower animal multiple, but a pathological monstrosity does not appear unless the twins are fused in greater or less degree. These double forms arise from a single ovum and germ vesicle and imply doubling of the embryonic area in a single blastodermic vesicle, with later coalescence, perhaps due to the entrance of two spermatozoa through the same micropyle; or two primitive streaks and medullary grooves, which may blend; or a medullary groove partly or wholly double; or a multiplication of parts late in fetal life; the first three explain abnormalities in the parts of the main somatic axis, the variations of the latter kind lie outside.

Common Anomalies.—Adequate treatment of the subject of teratology is impossible in a compend of this size; all that can be done is to mention the commonest anomalies.

The Heart may be deficient in part of the septum, making an organ of two chambers, like the fish's heart, or of two auricles and one ventricle, like the reptilian type; or one or more valves may be defective or redundant, stenosed or dilated; or fetal channels may persist, with general cyanosis as the result; or the aorta may be hypoplastic, with imperfect development of the lower half of the body; or the entire heart and main blood channels may be transposed.

The Lungs and Liver seldom show important abnormalities. They may have fewer or more lobes, thus the right lung may have two or four and the liver may have four; the liver may also present vertical furrows on its superior aspect, which are often congenital and have received the name of Zenker's furrows.

The Kidneys often show the remains of fetal lobulation. They may be united at the lower poles by renal or fibrous tissue, or one organ may be so small as to be functionally inactive, the other being correspondingly large.

The Alimentary Canal shows imperfect closures at the oral end, usually along the line of the premaxillary suture, involving

only the lip and then called harelip or running through the roof of the mouth also and known as cleft palate ; remains of the omphalo-mesenteric duct, known as Meckel's diverticulum, a small pouch from the free aspect of the ileum about three feet above the ileo-cecal valve, free at its distal end or connected with the umbilicus by a fibrous cord or an open channel ; hernias in various situations, which are not due to defect in the canal but rather to incomplete abdominal walls ; various degrees of imperforate anus, due to imperfect involution of the integument to meet the hind gut.

FIG. 1.



HYPOPLASIA CEREBRI. (Ziegler.)

a, Right hemisphere; *b*, left hemisphere; *c*, left occipital lobe, showing microgyria; *d*, fluid collection covered by membrane, region of temporal lobe. From a deaf mute.

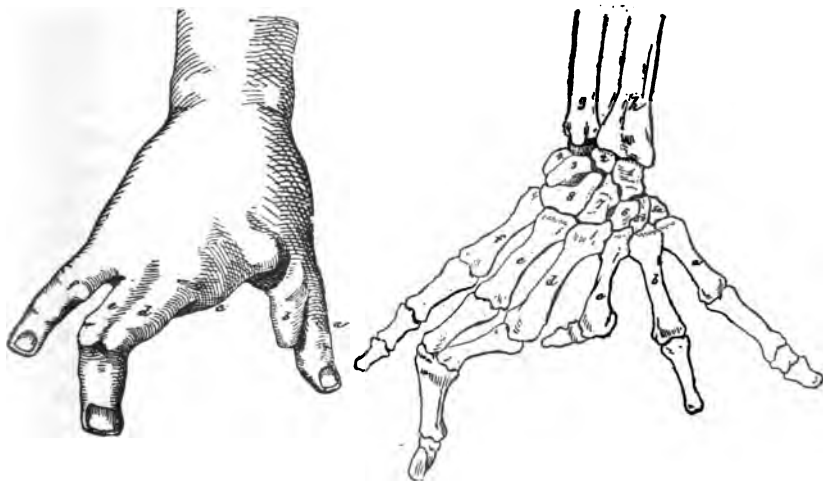
The External Genitalia may be malformed from non-union of parts in the median line, causing epispadias and hypospadias in the male, marked degrees of which sometimes pass for hermaphroditism, extroversion of the bladder in either sex, bicorn uterus and double vagina in the female.

The Nervous System may present anomalies of the organs or of the enclosing canals or of both. If the neural groove fail to complete its posterior half the spinal cord is exposed making spina bifida in its varying degrees, or the nervous tissue may be represented by rudimentary and imperfect nerve strands and ganglia. Frequently the defect of the canal allows the contents to escape, making syringo-myelocoele if the central canal of the cord is dilated, myelo-meningocele if the hernia is from the neural canal alone, encephalocele if from the cranium and containing brain tissue, encephalo-meningocele containing brain and fluid, meningocele, containing fluid alone. In all these cases there is a tumor connected with the spinal column, usually presenting posteriorly through the imperfect bony arches, lined more or less completely by dura and pia with or without nervous tissue, and containing varying amounts of cerebro-spinal fluid. The most pronounced degree presents a shallow groove (the posterior half entirely absent), with no brain or cord (anencephalia and amyelia), but such monsters are incapable of independent existence and are of only scientific interest. Defects arising after the spinal canal and cranium are formed lead to small brain and cord (micrencephalia and micromyelia), small or absent convolutions; clefts or depression in the cortex, the place being filled by excess of fluid (porencephalia); similar excess of fluid within the ventricles or over the cortex, known as congenital hydrocephalus.

The Skeleton presents absent, deformed, and imperfect bones, often traceable to pressure during fetal life; the limbs may be absent from non-development, or from intra-uterine amputation by amniotic bands; variously blended, and redundant in the double forms. The digits are frequently increased or diminished

in number and variously misshapen ; extra digits are often associated with extra teeth and show strong heredity.

FIG. 2.

MALFORMATION OF THE RIGHT HAND. (*Ziegler.*)

Perochirus with fusion of digits ; *a*, extra thumb ; *b*, normal thumb ; *c*, index finger. *d-f*, the other three fingers.

Skeleton of Perochirus ; *a-f*, as before ; *g*, ulna ; *h*, radius ; *5a*, extra trapezium ; *5b*, normal trapezium. The other figures refer to normal carpal bones.

Double Monsters are of two main varieties ; either the twins are of the same size and degree of development, or there is marked discrepancy between them. Instances of the first kind may be capable of extra-uterine life ; the same is sometimes true of the second variety. They are named in the first variety by adding to the part by which they are joined the syllables *pagus* (from radicle *pag*, meaning to fasten). Thus a pair of twins joined by the thorax are called *thoracopagus* ; if by the heads, *cephalopagus* ; if by the lower buttocks, *ischiopagus*. These forms frequently have their internal organs so separate and well developed that their association is little more than an in-

convenience. When one of the twins is much larger than the other it is called the autosite and the smaller is the parasite ; the

FIG. 3.

ISCHIOFAGUS. (*Ziegler.*)

latter is usually very imperfect in some important region or organ.

CHAPTER III.

DISORDERED BLOOD-SUPPLY.

Normal Circulation.—The circulation is divided into the greater and the less, or the systemic and the pulmonary, and the conditions in the two are not identical. The blood flow through the systemic and larger division depends upon five factors: The active contractions of the left auricle and ventricle; the arterial recoil, especially marked in the aorta and its main branches; the caliber of the arteries and arterioles, dependent in great part upon vasomotor influence; passive compression of the veins by the muscles among which they lie; and the inspiratory hiatus which determines blood from the large venous trunks toward the right side of the heart. Interference with any of these may cause local or general disturbance of the circulation. A subsidiary department of the systemic circulation in which disorders are common is the group of veins known as the portal, which from their anatomical relations offer many peculiarities. The flow through the lesser circulation is due chiefly to the activity of the right auricle and ventricle, aided by the movements of the thorax and the difference in pressure between the two circulations. The blood-pressure is high in the aorta, owing to the elasticity of its walls and the resistance of the countless subdivisions of the arterial tree; in the capillaries it is less and in the veins, except when gravity acts upon a long column of blood, it is very low:—normally it is least in the pulmonary circulation. As there is no method of accurately measuring the pressure in the capillaries we can say merely that it must vary according to the conditions in the arteries and the veins; if the arterial supply increases without change in the veins, it must rise, and *vice versa*.

Causes of Variation.—*Disorders of circulation* may be local or general, and are the result of many and varied causes. Thus altered cardiac function may be either muscular or valvular. If muscular we may have *excessive* or *diminished* action. Overaction is less common than its opposite, and usually temporary; it raises the blood-pressure, the quantity of blood in the vessels and the rate of flow; if the vessel be diseased these may combine to produce hemorrhage. Such increase of frequency and force in the heart's action may be due to emotion, muscular action or drugs, in all of which it is usually temporary. With prolonged excess in eating and drinking overaction becomes habitual, with hypertrophy of the heart, bounding pulse and flushed face. In certain diseases, as exophthalmic goitre, there is tachycardia with consequent hypertrophy of the left ventricle. Slight degrees of increased action lead to heightened glandular and mental activity; if prolonged, to headache and insomnia.

Diminished power and frequency in the cardiac function are common and important in results. The frequency may be lessened with increase of power by certain drugs, of which digitalis is the typical example, but as a pathological condition we usually find both force and frequency decreased. This may be due to fatigue of the muscle fibers from overaction, as the result of high fever, from poison of various kinds, in starvation and anemia and following changes in the coronary arteries. These and other causes may lead to degeneration of the heart muscle, the cells being cloudy or fatty, or holding pigment, or in great part replaced by new connective tissue; when the coronary arteries are at fault, we may find atheromatous plates in them, narrowed caliber and degenerative changes in the territory of distribution. Such weakened action is frequent with valvular lesions, pericardial effusion and adhesions, new growths of heart and lungs, vesicular emphysema, cardiac thrombosis, etc. Whichever valve is involved, or however the heart may be weakened, the result is an abnormal collection of the blood in the lungs; with lesions in the left side of the heart the

blood is dammed back through the mitral and into the lungs, if on the right side, the chief agent for the pulmonary circulation is eliminated with the production of pulmonary congestion. If the left side alone is involved, the right remaining vigorous, the venous congestion is not systemic ; as soon as the right ventricle becomes weak also, there is general passive venous hyperemia. As results we find that the arterial pressure falls, the circulation is slowed, nutrition throughout suffers, with cyanosis, edema, cold extremities, etc. The pulse wave is weak and slow, and if the heart is slow enough the arterial system has time between beats to nearly empty itself from the arterial recoil.

Valve Changes.—The disorder of the heart function may begin as a valvular lesion and any one or more of the four valves may be affected, in the order of frequency, mitral, aortic, tricuspid and pulmonary ; in time the muscular tissue is always involved also. As far as the circulation is concerned the result is passive venous hyperemia. (See Part II., Chapter II.)

Vasomotor Phenomena.—The caliber of the smaller vessels is controlled partly from cerebral centers in medulla and pons, the fibers passing down the cord and out through the anterior nerve roots to the sympathetic, and partly from centers distributed along the cord. Anemia of the nervous tissue, especially of the medulla, and highly venous conditions of the blood cause increased activity of these vasomotor centers, general vasoconstrictor action and acceleration of the blood flow. Their activity is heightened by some afferent impulses, with a rise in the blood-pressure, and depressed by others, when pressure falls : local effects of stimulus are frequently made up of both these phenomena, a constriction with anemia followed by a dilatation and hyperemia, or vice versa ; the mechanism in the region of face and head being very much under the control of the emotions, as seen in blushing, and in anger of the red and the pale forms. Certain toxic actions, from poisons introduced or manufactured in the body, as in the coma of alcoholism and of uremia, may be associated with profound vasomotor effects, with correspond-

ing pallor or flushing of the face and injection of the conjunctivæ. In scarlet fever it is not uncommon to see the entire bodily surface a brilliant red color and the face absolutely pale, the two representing the extremes of vasomotor action. In nearly every irritation it is usual to have a strong constriction followed by a marked dilatation, as seen in holding a piece of ice, the hand being first cold and anemic and then red and hot and hyperemic (similar changes occur in the other hand); which explains why eating snow and ice will not quench thirst, the subsequent hyperemia of the throat aggravating the condition. In the beginning of most inflammations there is first a constrictor effect with hurried circulation and then a dilated condition, with hyperemia, pulsation, subjective throbbing and increased temperature; of the two the second, or dilatation, lasts the longer. There is a well-developed compensatory mechanism between one region of the body and another by means of this vasomotor circle, of the greatest importance in defense of the body and in disease processes. Thus a scald or burn of the surface may cause vasodilator effects along the alimentary canal, which may lead only to increased functional activity of the mucous membrane or to ecchymosis and subsequent digestion of the part involved, with the production of an ulcer. Severe pain and extremes of mental emotion may lead to such dilatation of the abdominal vascular region that it will contain the greater part of the total blood, with consequent cerebral anemia which produces syncope and prevents death from excess of pain, or, if of higher degree, causes it by intravascular hemorrhage, the patient bleeding to death into his own portal system. After injuries to the genital organs and operations about the pelvis this condition of shock is fairly common. Some of these vasomotor effects are physiological and compensatory, as when one of a pair of organs is incapacitated and the blood-supply of the other rises with the necessity for increased function; certain of them are only pathological, as when the inhalation of CO_2 causes general contraction of the arterioles, increased blood-pressure, lessened

heart activity and venous congestion. In skin disease vasomotor effects are of prime importance, *e. g.*, herpes, urticaria and erythema, the rose rash of primary syphilis and other exanthemata.

Volume Changes. *General Hyperemia and Anemia.*—Increase in the total volume of the blood is possible by salt infusion and by transfusion, mediate or immediate, but it seldom persists for any long time, for the renal, sweat and other glands eliminate it very fast, and any excess may be temporarily stored by means of vasodilatation, usually in the abdominal region. Where excess in food and drink is habitual, we may find the condition known as plethora, with resulting cardiac hypertrophy (left ventricle), flushed face, general obesity, and hyperemia of the cerebrum, evidenced by headache and bad temper. A decrease in the total volume, general anemia, is also most commonly temporary, and is seen after loss of blood; if large, this may cause death by cerebral anemia; if smaller in amount, the deficiency is soon made up by absorption of fluid from the tissues, decreased excretion and increase in fluids ingested. This variety of anemia, to be distinguished from essential anemias of every grade, is accompanied by lower pressure and pulse rate, and, if persistent, by imperfect filling of the arteries, cardiac atrophy, dry skin, emaciation and torpor, as seen in starvation and those forms of it called cachexia. When the total amount of blood is diminished it is called *oligemia*; when the fluid part is chiefly affected it is said to be *anhydremia*. The capacity of the venous system is normally far greater than that of the arterial, but from hypoplasia of the arteries this disproportion may exceed the usual limits, and there is then a relative anemia on the arterial side throughout life, with corresponding ill-development of part of the body, usually of all below the umbilicus. Imperfectly developed arteries, disease of the intima, rigidity of the vessel walls, arteriofibrosis, as seen in kidney disease, aortic stenosis and aneurysm, all may cause increased resistance in the arteries and consequent diminution of their blood capacity and anemia on that

side of the circulation. Similarly, vascular dilatation in the arteries may increase the amount of blood in them, lessening the disproportion between arterial and venous capacity and depriving the venous current of its normal *vis à tergo*, tending to general stasis and death.

In the lesser circulation deformities of the thorax, thickened and adherent pleura, effusions into the pleural cavities and vesicular emphysema tend to increase intra-vascular pressure and hence also the effort of the right side to empty itself in systole, producing work-hypertrophy of the ventricle, regurgitation through the tricuspid and dilatation of the auricle. Occasionally such mechanical obstacles in the thorax cause backing up of the blood into the main venous channels, venous pulse in the neck, cyanosis and visceral hyperemia.

Local Hyperemia, Active.—Any portion of the body may have within it more than the physiological allowance of blood; the condition is called hyperemia and may be arterial and active or venous and passive. In health no part of the body contains its entire capacity of blood, but physiological activity is associated with and dependent upon increased supply due to vaso-dilator action in the afferent arteries, to be followed by constriction and relative anemia, the entire cycle marked by a rhythm peculiar to the special organ or part. Increased persistent physiological hyperemia may pass the bounds of the normal and sometimes depends upon loss of function in a neighboring part, as in one of a pair of organs; excessive stimulation of the vaso-constrictor fibers, active stimulation of the vaso-dilators and injury of the vascular muscle fibers, all have in the end the same effect of causing active hyperemia, which explains many contradictory drug actions through paralysis by overstimulation. Sudden removal of support may cause active hyperemia in the vessels of various parts, as when a large amount of residual urine is incautiously withdrawn and hemorrhage follows from the vessels which had become accustomed to its pressure. So also the relief of pressure anemia is followed by hyperemia, as when a tight

shoe by its removal allows the part to be filled by blood, with consequent growth of the corn which is the joint result of intermittent pressure and blood supply.

Whatever the cause, the signs of active hyperemia are bright red color, slight swelling, subjective warmth and throbbing, local rise of temperature, with perhaps discomfort and pain; the function of parenchymatous organs is increased, muscular power of work is increased with hypertrophy of substance, mental activity may rise or there may be headache or insomnia, excitement, and delirium. The tendency of active hyperemia is first to hypertrophy of the part and second to inflammation. Temporary active hyperemia may leave no postmortem evidences, except where the circulation is peculiar, as in the kidney.

Local Hyperemia, Passive.—Due to imperfect emptying of veins, capillaries and smallest arteries, caused by pressure on a large venous trunk, as by a tumor, dislocated bone, the gravid uterus, or thrombosis of veins, often aided by gravity and the mechanical disposition of the part affected, as in the hyperemia of dependent parts of the lungs in feeble patients. Or there may be more general causes, as cardiac valvular lesions with partial arrest of arterial circulation and regurgitation of venous blood, obstacles in the lesser circulation, as emphysema, extra intrathoracic pressure as from violent muscular exertion, playing wind instruments, etc. When chiefly mechanical and due to gravity it is called hypostatic. In its highest degree venous hyperemia is known as *stasis*, the circulation through the part being nearly or entirely inhibited. The signs of venous hyperemia, especially marked when local, are bluish or cyanotic color of the surface, swelling and edema, lowered function and temperature, and a tendency on the part of the blood to escape from the vessel, the fluid exuding first, then the white cells and lastly the red. If persistent and not too marked, venous hyperemia is followed by degeneration of the higher cells of the part and replacement by new connective tissue, simply

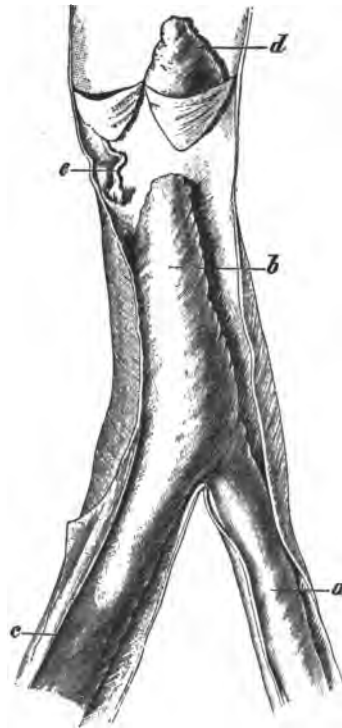
because connective tissue, historically among the first evolved, is the only tissue of low enough vitality to thrive in such unfavorable conditions, in which highly specialized cells of more recent acquisition and more sensitive nature, undergo fatty degeneration. In higher degrees the entire nutrition of the part suffers and there is necrosis and gangrene. The new formation of connective tissue is sometimes mentioned as a productive inflammation, but strictly it is a connective tissue replacement and to be regarded as an effort toward repair. If the part recovers from the hyperemia, especially if it has lasted a long time, the cells in the neighborhood and the adjacent lymph nodes may contain a large amount of pigment.

Local Anemia.—An active local anemia might be described, being a vaso-constrictor effect and usually without pathological significance. Distinguished from that, any other local anemia might be regarded as passive, caused by faulty distribution of the blood, as in shock, weak heart, atheroma, thrombosis and aneurysm of an artery shutting off its blood, pressure on the artery by organizing connective tissue or tumor; certain drugs, as ergot, and certain nervous influences may also cause a local anemia. If a collateral circulation develops soon there may be no permanent results, but in some arteries, known as end arteries, the only collateral circulation may be through capillaries and very slow in developing. From the disturbance of pressure in local vein and artery there may be regurgitation of blood from veins, stasis in the part and a red infarct; without such regurgitation a white infarct may form. Pallor, low temperature and loss of function are the direct results; degeneration, atrophy, and dry gangrene may be the ultimate.

Stasis.—When the circulation of a part is nearly or quite at a standstill the blood has the venous character and soon undergoes changes; the watery part oozes out of the capillaries, the cells partly wander out and partly fuse into a homogeneous mass; such changes are frequent in areas of inflammation and special microorganisms seem to have a peculiar power to produce them.

They may follow exposure of serous membranes to the atmosphere, too long applications of heat and cold, especially if with moisture, and also action of certain acids and alkalies. Three

FIG. 4.



OBLITERATING THROMBOSIS OF FEMORAL AND SAPHENOUS VEINS. (*Ziegler.*)

a-b, main thrombus, mixed and laminated; *c*, secondary peripheral red thrombus; *d*, valve with protruding thrombus.

factors enter into the local effects, the pressure within the vessels and in the tissues, the impaired nutrition of the part and the failure to remove the katabolic products of the cells. The results are seen as edema, diapedesis and hemorrhage, loss of func-

tion, atrophy and degeneration of higher cells, coagulation necrosis and gangrene. The cells undergo simple solution or fragmentation, in some cases with necrosis of the capillary wall and then of the tissue, with or without thrombosis in the veins.

Thrombosis.—Clotting of blood occurs in the heart and vessels as a regular postmortem change in the great majority of dead bodies, and the change is analogous to those observed in blood drawn during life and examined through several hours in vitro. The mass of red fluid separates into two parts, one, the serum, yellow in color, holding the water, salts and albumin which were in the blood, the other, the clot or coagulum, made up of red cells, white cells and fibrin. On false analogy the production of a solid body from the blood and in the vascular system during life was called a thrombus and defined as an antemortem clot formed in the vessels, the process being termed thrombosis; the conditions are not the same as in clotting outside the body and the make-up of the thrombus is not that of a coagulum. A thrombus is a solidifying body formed during life within a blood channel from fibrin, blood cells, and blood plates in varying proportions. It may be *red* when developed from stagnant blood, *white*, *laminated* or *mixed* when formed in a current. The thrombus in the first case contains both red and white cells entangled in fibrin, which is arranged in granules or threads often disposed radially about apparent centers. The *white* consist chiefly of fibrin and white cells and blood plates; thrombi of blood plates alone do occur, the plates being the result of precipitated globulins or derived from the red cells, and may be the first step in the production of one of the ordinary thrombi. Under the microscope the cellular elements and the fibrin in granules or rays may be readily recognized, and hyaline areas are often found, representing altered plates. The immediate cause of the thrombosis is the interaction between fibrinogen and fibrinoplastin (paraglobulin) under the influence of a ferment and in the presence of a calcium salt. The ferment may come from the white cells, from the erythrocytes or from the vessel wall, and

has been supposed to be phosphoric acid or nuclein containing phosphorus.

Causes of Thrombosis.—The factors leading to such a thrombosis are three, all pathological and often associated, namely, *changes in the vessel wall* especially in the intima, *slowing of the current* and *changes in the blood*.

Lesions of the vessels do not cause thrombosis until the endothelial lining is affected. Mechanical injury, as torsion and ligation, the formation of atheromatous plaques and ulcers, toxins due to bacteria, impaired nutrition and degeneration of the lining cells, phlebitis and arteritis are the most common causes; they all probably release fibrin ferment and increase the tendency of some of the elements of the blood to cling to the vessel wall.

The blood-current may be retarded or stopped by pressure from without, by foreign bodies and parasites in the vessel, by weak heart action, often associated with gravity, by aneurysmal dilatation with consequent eddies and areas of slow flow and rough surfaces; and emboli always lead to the formation of thrombi when they lodge.

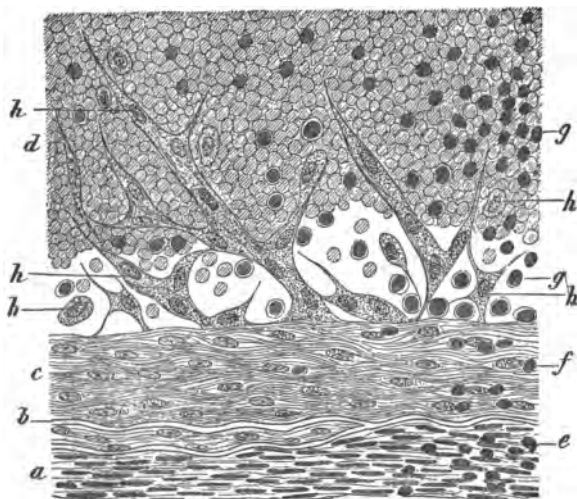
Under the third head, of altered blood, we note the tendency toward coagulation in pregnancy, in rheumatism, diphtheria, and typhoid, with other cases of prolonged high fever, from microorganisms and their toxins, and from increase in the number of blood-plates as in some essential anemias. Calcium salts and nuclein favor coagulation; oxalates, oily substances, sodium fluoride and albumose tend to retard it.

Varieties.—Thrombi are called from their
color, red, white, gray, or mixed;
structure, laminated and stratified;
time of formation, primary and secondary, the latter said to be propagated;
shape, situation, action, infection, etc.:
 obstructing, if vessel occluded;
 valve, if current permitted;

parietal, as on wall of aneurysm ;
 annular, in ring form ;
 canalized, if blood channels through it ;
 ball, if detached ;
 surgical, after ligation of vessels ;
 cardiac polypi, attached to heart wall ;
 fibromatous, if partly organized ;
 marasmic, formed in the course of asthenic diseases ;
 simple or aseptic if free from bacteria ;
 infected, septic, or putrid if with bacteria ;
 arterial, venous, portal, capillary, according to vessel
 involved.

Further Changes.—The commonest results in case of simple thrombus are shrinking and drying, alteration of the blood-pig-

FIG. 5.



ORGANIZING THROMBUS 3 WEEKS AFTER LIGATION OF AN ARTERY. (Ziegler.)

a, media; *b*, elastic layer; *c*, intima, thickened by productive inflammation; *d*, coagulated blood; *e*, cells infiltrating the media; *f*, the same in the intima; *g*, round cells in thrombus and between it and vessel wall; *h*, various forms of new connective tissue cells.

ment with change of color in the mass, and final organization ; if lime salts are deposited in it we find a phlebolith, arteriolith or, rarely, cardiolith, according to the site of the process. The center of the thrombus, being least supplied with nourishment, may soften, burst and be washed away, permitting the return of the circulation, the softened portion being a reddish-gray syrupy fluid made up of fat, albuminous and pigment granules which may be too small to cause appreciable embolism. If the thrombus is infected this softening is the usual course and the result is multiple infectious embolism with miliary abscesses wherever they lodge. In the organization of the simple aseptic thrombus the fibrin is pierced by new vessels from the vasa vasorum which carry new connective tissue with them and so gradually replace the fibrin. This new tissue then contracts and at a later date we have only a small fibrous nodule which may be hard to recognize as a former thrombus. Quite commonly a portion of the proximal end of a thrombus is torn off by the blood current, the thrombus always forming up to the nearest collateral branch, and the portion is then carried till it enters a vessel too small for its passage ; it comes to rest, plugs the vessel and is termed an embolus.

Results of Thrombosis.—

In vessel, organization :

softening ;
abscess, if infected.

In general circulation :

according to rapidity of formation ;
nature and size of vessel ;
establishment of collateral circulation ;
force of the current.

In the tissues, if in artery :

anemia till collateral circulation ;
infarct, red or white ;
death of tissue, dry gangrene.

If in a vein :

passive hyperemia, stasis ;
hemorrhage ;
edema ;
dropsy ;
moist gangrene.

Embolism.—This term is applied to the plugging of a vessel by a foreign body, which may be a piece of a thrombus from a larger artery or vein, coagulated fibrin from a heart valve, fluid fat from a recently fractured bone, air drawn in through the veins, fragments of neoplasms, pigment from disorganized hemoglobin, parasites and microorganisms, hyaline material after extensive burns, dust and mineral matter ; the most common are small blood clots, and the seat of arrest is often at the bifurcation of the vessel. If the foreign body comes from the veins or the right side of the heart it is usually caught in the pulmonary circulation, though a *retrograde* embolism, as of the hepatic vein, may be caused by convulsive action of the thoracic muscles and the diaphragm, which by extreme increase of intrathoracic pressure drives the venous current in the great veins in a reverse direction. From the left side of the heart an embolus is apt to lodge in the brain, often in the middle cerebral artery, or go on to the spleen or kidney ; embolism may occur in any organ and doubtless the peripheral are overlooked as their effects are less marked. If the foramen ovale is patent an embolus may be carried directly from the right side of the heart to the left without going through the pulmonary vessels, and pass into the systemic circulation, giving a *crossed* or *paradoxic embolism*. After fractures of the large bones of the limbs the fat set free from the injured marrow may lodge in the lung capillaries, causing *fat embolism* of the part and if in vast quantity, asphyxia and death. Air drawn into the veins may also lodge in the pulmonary capillaries, but unless in large amount may not cause any symptoms ; when fatal it is because the froth in the right

side of the heart gives it nothing to contract on and stops the circulation, causing irregular cardiac action and death. Neoplasms are often carried from one organ to another by means of small emboli, as when an ulcerating carcinoma of the stomach opens small radicles of the portal veins, causes malignant thrombus in situ and thence small fragments are borne to the liver, setting up a new carcinoma wherever they lodge. Dust, flour, clay, metal particles and other minutely divided foreign matter may be inhaled and laid away by phagocytes in the bronchial lymph nodes; if one of these softens and breaks the foreign material may cause capillary embolisms passim, leaving the body at last by way of the liver and the intestinal glands.

The *results* of an *embolism* vary with the importance of the part affected. If the vessel is a coronary or cerebral artery death may be immediate, as also after large pulmonary embolism; if small and soft the embolus plugs the vessel completely, if harder, only after thrombus develops about it. The territory supplied becomes anemic with loss of heat and function; this may be relieved by a collateral circulation: if not relieved we may find infarction or necrosis, and if the thrombus is septic, abscesses surely develop.

Portal embolism may develop after dysentery, simple or amebic, carcinoma in any part of the alimentary canal, pyelephlebitis, etc., and the usual result is hepatic disease, because the embolus passes from smaller to larger veins until it reaches the portal subdivisions within the liver; as emboli from such sources are usually septic it is common to find hepatic abscess as the result of suppuration throughout the interlobular veins (pyelephlebitis).

Infarction.—Certain arteries do not anastomose and hence are called “end arteries,” as those of the retina, spleen, kidney, heart and brain, and still others have but imperfect and few anastomoses; if such a vessel is plugged by an embolus its cone of distribution becomes anemic and necrotic. The area is called an *infarct*, the process *infarction*. In gross appearance the infarct is cone or pyramid shaped, its apex in the tissue and its

base on the surface, which is raised above the general level if recent and slightly depressed if old. Infarcts may be *red* or *white*, and either may be *pyemic*. The white infarcts are formed as described and are of an opaque yellow-white or gray; the red are formed by the entrance of blood into the anemic area, either by reflux through the veins, pressure in the plugged artery being nil beyond the embolus, stasis of this blood and diapedesis; or the diapedesis comes from dilated capillaries along the borders and the cells enter along the slant height of the pyramid, in which case even in the red form the center is usually lighter than the periphery. The formation of red infarcts is chiefly a matter of relative pressures in artery and vein; with pressure at its lowest in the former the tendency is toward red infarcts. If not septic, the necrotic tissue may become organized and replaced by connective tissue, which contracts and dimples the surface, a more or less radiating scar with a certain amount of pigment or of calcareous deposit being all that remains. If the artery plugged is already the seat of disease, or if the embolus is infected with bacteria of less than the highest virulence, the vessel wall may be destroyed and an aneurysm formed, or necrosis of the tissues about may follow and abscess formation. Infarcts occur in the lungs when the circulation is very much slowed, and here the infarct may become infected secondarily from some of the bacteria inhaled.

Hemorrhage.—Strictly speaking, hemorrhage is the massive exit of blood from a vessel. If blood plasma alone leaves the vessel it is called a *transudate*, and causes edema; if the white cells pass out it is called *emigration* of the leucocytes; if red cells, it is *diapedesis*; in hemorrhage all three are lost; it may be on the surface of a wound, under or upon a mucous or serous membrane, into one of the body cavities or into the tissues. Hemorrhage is called arterial, venous or capillary according to the vessel, mixed or parenchymatous if from all, and is divided into two kinds, namely, by *rhexis*, when the vessel-wall is broken, by *diapedesis*, when it passes through the wall of a capil-

lary or small vein without rupture of the wall. According to their situation and size, they may be called :

Petechiæ, if under the skin and small as flea-bites ; *q̄ibices*, if long and narrow, like strokes of a lash ; *ecchymoses*, under the skin, of larger size, with but little destruction of tissue, and after injury ; *purpura*, in many small scattered spots under skin and mucous membranes ; *suggillation* or *suffusion*, when of large size, infiltrating the tissues ; *hematoma*, when large and forming a distinct tumor.

According to the cavity into which blood escapes, hemopericardium, hemothorax, hematomyelia, etc.:

According to the channel by which voided, hematemesis, hemoptysis, hematuria, etc.:

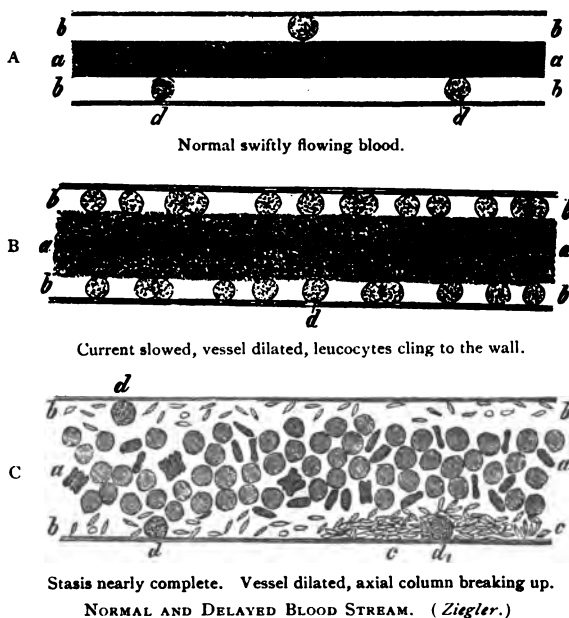
In brain, cord and lung, apoplexy of the part.

Simple outwandering of red or white cells, as seen in passive hyperemia, can not be called a hemorrhage, even though small hemorrhages per diapedesin can not always be distinguished from the former. The physical appearance of a hemorrhage depends upon the vessel from which it comes, whether a vein or an artery, but sooner or later in either case the blood extravasated into the tissue interspaces undergoes a regular set of changes, by which the red cells are broken up, their coloring matter altered into brown or black pigment and left in situ or absorbed, the white cells emigrate in small part or are destroyed like the red, fibrin forms, the clot shrinks, the area becomes walled off by a connective tissue capsule and itself organizes, all this new tissue contracts, lime salts may be deposited, and all that remains may be a small fibrous induration, somewhat pigmented. Large extravasation from an artery may remain in connection with the vessel, receiving new blood and pulsating with the arterial throb, and thus forming a false aneurysm.

The *cause* of *rhexis*, break in the vessel wall, may be injury from without or within, pressure on a wounded place as when a vessel is contused and breaks much later, disease of the vessel wall, removal of support, invasion by tumors and from diseases

of adjacent parts ; newly formed vessels and those in tumors are especially liable to break. The blood-pressure may be increased by violent heart action, obstacle to the venous flow, mental

FIG. 6.



a, axial stream ; *b*, lateral space, with occasional leucocytes in A, with many leucocytes in B, with blood plates added in C ; *c*, collection of blood plates ; *d*, *d*, white cells.

emotion, thoracic spasm as in coughing, asphyxia in the newborn and from other causes.

Diapedesis occurs through the bodies of the endothelial cells of capillaries and small veins or through the intervals between them ; the idea of stomata has been generally abandoned. It follows increased pressure and abnormally permeable vessel walls, from bacterial toxins, prolonged heat, and is seen specially in certain cachexias. The tendency to loss of blood, either

spontaneous or disproportionately large after injury, may be congenital, often hereditary, and is called *hemophilia*. A similar tendency may be acquired in scurvy, certain contagious diseases with high temperature, as typhus, malignant endocarditis, yellow fever, and in certain essential anemias, where the blood is disordered and the vessel walls suffer in their nutrition. The influence of the nervous system is strong in producing certain hemorrhages, as in hysteria with stigmata, vicarious menstruation with or without genital anomalies, disease of the brain, especially the crura, with bleeding in lungs or parts of the alimentary canal.

Effects.—Death may follow from the amount of blood lost ($\frac{1}{10}$ of the total volume); the patient may faint from cerebral anemia and recover with a slight fever, the heart action becomes slow and feeble, thus favoring clotting and control of the bleeding; the fluid lost is then made up by absorption from the tissues, stoppage of excretions, and ingested fluids. Repeated small hemorrhages may be fatal; single ones sometimes appear of benefit to the organism.

Lymphorrhagia, Edema, Dropsy. Loss of the contents of a lymph vessel is called lymphorrhagia. It is soon checked by counterpressure of the tissues unless on the surface of a wound or a serous cavity. Thus injury to the thoracic duct, either direct or secondary to other lesions, may cause extravasation of lymph into the pleura or the abdomen; and the presence of the tropical parasite *Bilharzia hematobia* in the lymph channels may cause escape of lymph into the bladder and hence chyluria, or milky urine.

From its frequency a far more important interference with the lymph stream is seen in the condition known as edema. White cells and the fluid part of the blood normally leave the capillaries for nutrition and repair of tissues. This fluid is the tissue lymph and is not identical with plasma, as is shown by the fact that it is often richer in salts and sugar, poorer in albumin, of lower specific gravity and does not coagulate spontaneously. Such a

fluid is called a *transudate*, to distinguish it from the fluid of ascites and *inflammatory exudates*. When such a process is excessive in the superficial tissues it is called *edema* and is most marked in lax and dependent parts, as the scrotum and the ankles; when general it is called *anasarca*. If the fluid accumulates in cavities it constitutes hydro-pericardium, hydrops articuli, hydrops abdominis or ascites or "dropsy." The belief that the serous cavities are expanded lymph spaces has been disproved by embryological study, and great as the analogy may be, collections of fluid in them are not the same as edema in the tissues. Their cause is usually hindrance to the venous return, *e. g.*, in the abdomen from atrophic hepatic cirrhosis and compression of the portal vein by newly formed connective tissue in the liver, or from cardiac valvular disease. The fluid differs in being far richer in albumin and of higher specific gravity; it may hold flocculi of fibrin in suspension, may coagulate spontaneously, and is often colored by the addition of blood or bile pigment.

Six factors enter into the production of edema, usually more than one acting at a time, *viz.*—positive pressure in the vessels (in proportion as it rises), permeability of the vessel wall, osmosis from excess of salts outside the vessel as seen in the action of a saline laxative, selective action of the endothelium, variations in the blood plasma, and obstructed onflow in the lymph channels.

We distinguish edema of active hyperemia; usually slight, though as a stage of inflammation it may reach a high degree, as in the lung.

Edema of passive hyperemia; the cause an obstacle to venous return, the classic example cirrhosis hepatis; also from heart disease, vesicular emphysema and obliteration of lung capillaries, or pressure from a gravid uterus with phlegmasia alba dolens; in all, a simple leaking from distended weakened vessels.

Edema from obstruction to lymph channels; as pressure on the thoracic duct, parasites in the channels; often lasts a long time without symptoms because of free anastomosis.

Edema of cachexia ; the blood being altered, nutrition of vessels impaired, combined effect is transudation.

Toxic edema, from action of microorganisms and their products on vessels and blood.

Inflammatory edema ; here the fluid is called an *exudate*, is rich in albumin and cells and coagulable.

Neurotic edema ; as in the vesicular skin eruptions, dropsy with neuritis and diseases of the cord, a trophoneurosis in most cases.

Whatever the cause, edematous parts are swollen, pit on pressure, if superficial have a lowered temperature, function at first less and then lost, fluid in the interstices and then cells and fibers of the part swollen, area disposed to fatty degeneration and necrosis. (See Coagulation necrosis.) In the organs, as the lung, the part is swollen, dense and pale, its histological elements are pushed apart, and on coagulating the fluid by boiling water it is found to be not only in the alveoli but also in the tissue spaces themselves. Such a tissue when cut exudes a large amount of usually clear fluid. If there is a prominent mucous element, as in disease of the thyroid, it is called *myxedema*.

SYNOPSIS OF CHAPTER III.

1. Altered blood supply from altered cardiac function. (a) Muscular—increased power and frequency, decreased power and frequency.

2. (b) Valvular—right side ; pulmonary, tricuspid : left side ; aortic, mitral.

3. Vasomotor phenomena—dilator, constrictor.

4. Volume changes—anemia, local and general, active and passive ; hyperemia, local and general, active and passive.

5. Stasis, coagulation, thrombosis, embolism.

6. Infarcts, hemorrhage.

7. Lymphorrhagia, edema, dropsy.

CHAPTER IV.

DISORDERS OF METABOLISM; CONSTITUTIONAL.

Metabolism is the collective term given to the entire series of physiological processes by which the organism acquires nutriment, prepares it for the nutrition and repair of its parts and rejects such elements as are not available. Obviously, then, metabolism, implying the activity of so many organs and the integrity of so many separate processes, may suffer such alterations at any one of the numerous stages as to become pathological. The abnormality may be one of function or of structure, usually the former precedes the latter and both coëxist by the time they become the object of study.

Metabolic disorders of the organism as a whole may occur along two lines, either in the nature of the pabulum supplied or in the use made of it. The pabulum may vary in either amount or quality, but it will be convenient to discuss it as either excess or defect.

If food and drink are taken in larger amounts and more frequently than is required for the bodily needs, the excess either passes out of the intestines undigested (its previous putrefaction may have serious consequences), or it causes an overfulness of the blood-vessels (plethora) or general increase of the body fat (obesity). Such persons are often characterized by ruddy complexion, prominent vessels and eye-balls, great activity, muscular or mental, copious defecation, high-colored urine and tendencies toward active congestion in various organs. On the other hand, when nutriment is supplied in too small quantity or poor quality, or what amounts to the same thing, the digestive powers cannot make use of good food, the bodily weight diminishes, its

heat likewise and all its energies, collections of fat and glycogen are consumed, except in the case of fatty new growths (from heart, kidney and nervous tissue last), respiration and pulse-beat become slow and feeble, the fluid part of the blood is lessened and its cells also, though they show a relative increase, secretions and excretions are less in amount and altered in quality, mental torpor alternates with delirium, and death occurs from exhaustion (*inanition*) or from the products of altered gland action. When similar conditions develop in the course of a definite disease it is termed a *cachexia*, and while all cachexias have starvation in common, they vary according to the effect of the concurrent disease; thus, we speak of *marasmus* in the newborn, *anemic*, *malarial*, *cancerous*, *suprarenal* and other cachexias. Starvation is understood to refer to food supply, but lack of oxygen in all its forms is also a starvation and manifests itself as air-hunger, dyspnea and cyanosis; local starvation ends in atrophy or necrosis.

Misuse of Pabulum.—Food taken, though of good quality, may be wrongly used, either in the anabolic or the katabolic series of changes; or there may be excessive tissue waste apart from the amount of food ingested. In certain cases the origin of the trouble may be sought in the alimentary canal or tributary glands, in others the emunctories are at fault and retain matters which are noxious in their effects.

Three chief types of such intoxication may be recognized:

1. Some important function may be impaired, with or without tissue changes, especially in the glands which destroy toxic metabolic products by further elaboration. As examples may be cited Addison's disease, acute yellow atrophy of the liver, myxedema and pancreatic diabetes.
2. Intermediate and toxic products of metabolism may enter the general circulation without any localized lesion, as in diabetes, gout, oxaluria.
3. Products of retrograde metabolism which should be excreted are retained in the circulation or the tissues, as carbonic

acid gas in dyspnea and carbon monoxide poisoning, various excreta in uremia. At times the formation of such products may exceed the ability to excrete them by the emunctories and this may be due to increased production or decreased elimination, with steady accumulation in either case, as in carcinomatous and diabetic coma, acetonemia, cystinuria.

Acid Intoxication.—From albuminous food both sulphur and phosphorus may furnish corresponding acids, lactic, sarcolactic, oxybutyric and other acids may be developed, and the excess in part neutralized by ammonium and fixed alkalies, in part split into other bodies, as acetone and diacetic acid; imperfect oxygenation usually coexists. The constitutional effects are disturbance of pulse and respiration, marked dyspnea, stupor and coma, as seen in diabetes; to a slighter degree such symptoms occur in many fevers, carcinoma, acute yellow atrophy of the liver, phosphorus poisoning.

Albumosuria.—Where there is rapid tissue destruction albumoses or peptone may form and appear in the urine; a certain excess of leucocytes usually accompanies the symptom, but the details of the condition are still obscure.

Intestinal putrefaction is a common result of imperfect use of food and leads to many of the well-known self-intoxications. The process is extremely complicated and more than one type may be recognized. Fermentation may occur in the stomach and causes the dissolution of carbohydrates; it may be of the acetic, butyric, lactic, or alcoholic form. Putrefaction occurs in the intestine and concerns proteids; its products are chiefly cystin and methyl-mercaptan, or amido-acids, or substances of the aromatic series, as acetone, cresol, indol, skatol and tyrosin. Ptomains are also present and may account for many of the symptoms. If food decays outside the body and is then eaten, it poisons by the ptomains in it; similar effects follow putrefaction in the gut. Many of the alkaloidal bodies of albuminous decay resemble strong vegetable alkaloids, strychnine, morphine, etc., and in the usual cases the patient may exhibit digestive and

nervous symptoms like those caused by repeated small doses of such drugs; if too irritating, an attack of diarrhea may result and relieve for a time. In more severe degrees, especially when the kidneys do not eliminate absorbed poisons, *copremia* results, with indican and ethereal sulphates in the urine, cold surface, cramps, convulsions, perhaps death in coma. The extract of 2.5 gm. of putrid feces is fatal to an animal weighing one kilo. In the chronic forms of slight degree, often with crises and exacerbations, the skin and mucous membranes are subject to inflammations of various kinds, melancholia and hypochondriasis often follow, and in the infant, rickets.

Icterus.—The bile contains fats, biliary acids and salts, soaps and cholesterin, and coloring matters; these latter are bilihumin, biliprasin, bilifuscin, bilifulvin, biliverdin, bilirubin.

These are all derivatives of the last, bilirubin, which resembles hematoidin, and in poisonous effects from bile resorption it is the coloring matters which are the chief element; bile deprived of the coloring matter by filtration through charcoal becomes one third as toxic as entire bile. The daily amount of bile varies from 800 to 1,200 cc. for the adult, enough to kill three men of average weight if injected into the veins, or enough in 8 hours to commit physiological suicide. The great safeguard against poisons from the intestine is the liver, which destroys them and excretes them into the duodenum again; against poisons circulating in the blood the kidneys perform a similar office of elimination. Normally the acid contents of the stomach on reaching the intestine cause a precipitation of the bilirubin in the form of insoluble granules; if from interference with its excretion a stasis of bile occurs in the liver it may gain entrance to radicles of veins or lymphatics and thus enter the general circulation. But that it is eliminated rapidly by the kidneys and the excess deposited in the tissues of the connective type, fatal poisoning in this condition would be more common. Cholemia may be considered also as an acholia rather than a hypercholia. Some urea is formed in the liver from ammonium car-

bamide, but with impaired hepatic function this is not formed and also certain poisons from the alimentary tract may slip through into the general circulation (arsenic, glyocol, amido acids). Recent opinion tends to consider the bile salts more poisonous than bile pigments.

Excessive Catabolism.—Apart from tissue waste in starvation, there may be extreme destruction of various cells in fever of any sort, new growths, especially carcinoma, Basedow's disease, phosphorus poisoning, and many other conditions. The cause of the great waste is partly the degeneration following high temperature, partly the accompanying disorders of cell nutrition, and at times the production of some toxic substance peculiar to the special disease. Such hypercatabolism is therefore a feature of many clinical pictures rather than a disease in itself.

Disordered Secretion and Excretion.—Here two groups may be recognized, with many transitions and combinations; cases where something of value to the organism is lost by way of the emunctories, and cases where excreta are retained. One of the most important cases of the former is *albuminuria*, the excretion of serum albumin and serum globulin by the kidney in consequence of damage in the glomerular and tubal epithelium of the kidney; this regularly accompanies various forms of nephritis and will be treated in that relation. If blood as such occurs in the urine it is called *hematuria*, if the blood pigment, *hemoglobinuria*; the former occurs most often when the urinary organs and passages are diseased, the latter when the circulating blood is affected and its red cells destroyed, as in malaria. *Dextrose* or *glucose* lost by the urine is the distinguishing symptom in *diabetes*, though it occurs as a transient symptom in some nervous diseases or even after large use of sugar and carbohydrates in the diet. Normally, the liver arrests sugar coming from the alimentary canal; if imperfect function allows some to pass we have an alimentary glycosuria or more persistent forms. Extirpation of the pancreas causes diabetes, for the regulative function of the gland is removed and more sugar reaches, and passes, the liver.

In the blood sugar is a protoplasmic poison, causing increased catabolism and nitrogenous elimination.

A good example of retained excreta is furnished by *uremia*. The daily amount of urea excreted in health varies from 30 to 40 grams, and its retention was supposed to cause the symptoms grouped under the name of uremia. The urine contains seven or eight toxic substances which have been recognized, among them one which causes lower temperature, one causing myosis, one causing coma, as well as potassium, a tissue poison, urea and other organic poisons. No one of these will produce experimentally the features of human clinical uremia and it is probable that the condition is due to imperfect excretion of urine as a totality rather than to a single ingredient, which may account for the many forms of uremia as one or another element prevails. In pregnancy the urine becomes less toxic, the serum more so, hence puerperal eclampsia may be a retention-toxemia. But it has been supposed that the fetus may elaborate a substance toxic for the mother, for the case at times differs from other uremias.

In Addison's disease the intoxication may be due to the absence of the regulating influence of the adrenals on the neurin in the body, as the thyroid may be supposed to affect the metabolism of mucin and the pancreas that of sugar; but severe lesions of the adrenals may be found with no history of suprarenal melasma, and the intoxication may exist without characteristic changes in these organs.

Connected with the thyroid gland four conditions are recognized, cretinism, myxedema, cachexia strumipriva and Basedow's disease; in the first three the function of the gland is imperfect or lost, in the last the picture is rather that of extreme activity. Thyroid gland supplied in the first three usually relieves the symptoms, in the last it aggravates them and it may produce similar manifestations in the healthy. Three explanations are offered for these conditions: Either the gland produces a toxic substance from morbid function, or the normal product is ex-

cessive, or the gastro-intestinal tract prepares a toxic substance from mucin because of impaired control by the thyroid body.

Oxaluria and *phosphaturia* are conditions of the urine when it holds an excess of oxalic acid salts (calcium) or of phosphates. Both occur as an expression of defective metabolism and tissue waste, in dyspepsia with imperfect carbohydrate digestion and retention of intermediate products, nervous functional disorders, and bone diseases.

Acetone and *diacetic acid* in the blood and urine are often found in the later stages of diabetes and hence are of grave clinical significance.

Uric acid retained in the system is closely connected with gout.

Hydrothionemia is occasionally seen, due to the presence of sulphuretted hydrogen in the blood ; this gas can be recovered from both urine and feces.

APPENDIX TO CHAPTER IV.

Fever.—Clinically the essential symptom in fever is elevated bodily temperature, but with that the heart action is increased in force, frequency, or both, the process of respiration is involved and the urine shows the effects of increased tissue waste. When the normal balance between heat production and heat dissipation is lost we may have lowered or elevated body temperature as the result ; if high, the temperature is a *fever temperature*. The normal temperature of the body is stated as 98.8° F. (37.2° C.), with daily variations of perhaps a degree less in the early morning and a degree higher in the evening, and in fevers these variations are often reproduced on a higher level. *Moderate fever* runs between 101° F. and 103° F.; any temperature over 105.5° F. is called *hyperpyrexia*; such very high temperatures are seen in exanthemata, pyemia, sunstroke, and occasionally in hysteria. The nature of fever is still obscure in many points. The source of the high temperature may be chemical rearrangements of the ultimate elements of body cells and consequent liberation of

energy in the form of heat. The *etiology of fever* includes insolation, nervous disorders, infection by various microorganisms and the effect of their ferments and toxins. Its *results* are emaciation, degeneration of glandular and muscle cells, loss of function in any structure, and death from the tissue change or the retention of excreta; recovery is possible as long as the violence and extent of such alterations are relatively limited.

Many fevers present well-marked stages in their development:

Initial stage, the temperature rising to the height characteristic of the special disease, usually in a few hours; if sudden, accompanied by a chill, which is an expression of disordered innervation, an explosion of motor energy setting the muscles, voluntary and involuntary, into irregular, convulsive activity; the chill begins usually with vaso-constrictor spasm of peripheral arteries and subjective coldness.

Stage of Acme, or Fastigium.—Temperatures fairly stationary about a daily average, with slight morning fall and equal evening rise.

Stage of Defervescence.—Fever temperatures returning to the normal rapidly, with general improvement, often accompanied by sweating, said to end by *crisis*; where defervescence is protracted over days, by *lysis*.

Typical typhoid fever shows these stages very clearly, the curve for the four weeks being roughly described as, "first week staircase, second week stationary, third week remittent, fourth week intermittent."

The cyclical nature of many fevers is perhaps to be referred to the death of the causing organisms after they have exhausted the substances in blood and tissue which are available for their nutrition, or after their products reach a percentage beyond which they inhibit the growth of the producing organisms, or after the body cells have produced a substance which is fatal to the organisms; the subject is entirely a matter of supposition, but the self-limited nature of many fevers is one of their clearest characteristics. (See Immunity, Part II.)

CHAPTER V.

DISORDERS OF METABOLISM ; LOCAL.

DISORDERS of metabolism may be *local*, and then we find that the disorder is either *quantitative* or *qualitative*. Local metabolism disordered quantitatively may err either in excess or defect ; as excess we have hypertrophy, hyperplasia, and metaplasia ; as defects we have agenesis, aplasia, hypoplasia and atrophy.

Hypertrophy.—The term hypertrophy is applied to the increase of a part with increased function, without departure from normal structure or chemical composition, and it may be physiological or pathological. The significance of the term is often relative, a kidney weighing six ounces being normal if found in an adult but hypertrophied in a child, and it may be difficult to define the limit beyond which the size and weight of a part justify the name. In a hypertrophied tissue the various elements are supposed to be larger than normal (uterus at term), without numerical increase, and hyperplasia is reserved for the latter condition ; the distinction is not of great value in the physiological hypertrophies but perhaps has significance in the pathological ; thus the more numerous bile ducts in atrophic cirrhosis are strictly a hyperplasia.

Hypertrophy may be congenital, manifested as a giant growth of the whole body or a part of it, or it may be more localized to one form of tissue, as skin, hair and nails ; or such extra growth may develop in after life without apparent cause, as in the case of cutaneous horns. Other cases of hypertrophy may be traced to heightened functional activity, as in the muscles of the athlete, the waste of the muscle cells being more than made up by extra

nutrition and this excess manifesting itself as increased size. Certain forms of hypertrophy are called *compensatory* and certain others might be called *vicarious*, an example of the first being furnished by one of paired organs which takes up the function of the other and with the greater activity increases in size, and a good instance of the second is found in the tactile development of the blind.

Pathological hypertrophy is usually due to irritation and its sequel, inflammation, or it may be compensatory, as in the cardiac ventricles when they have to overcome increased resistance due to lung and valvular changes. A simple case of the effect of irritation is seen when intermittent pressure and friction increase the thickness of the epidermis; certain inflammatory discharges also will cause local hypertrophy of the integument, as warts and condylomata. When larger areas of integument are involved, as in elephantiasis, the part may reach many times its normal size. The spleen and the lymph nodes enlarge in some forms of constitutional disease, perhaps in part from overwork, and distal portions of the skeleton may hypertrophy, as in the disease called acromegaly, with or without alterations in the hypophysis cerebri. At times the response to irritation is hyperplasia, numerical increase, though the new formations are not larger than normal, as seen in the new bile ducts of cirrhosis.

Metaplasia is the name given to the alteration of a tissue into one of another variety and is a term of very limited application, confined almost wholly within the borders of the connective tissue group. Thus hyaline cartilage may become fibrous, and mucous tissue may become adipose, and such changes are seen in both physiological and pathological processes, but epithelium never becomes fibrous connective tissue or vice versa, though columnar epithelium may become squamous. The altered tissue most often does not persist and the metaplasia may be considered as a stage of a degenerative process; in many cases it belongs in the qualitative disorders of metabolism.

Heteroplasia is the development within a formed tissue of a

new tissue foreign to that locality, though perhaps normal elsewhere, and while the effect is sometimes increase of the size of the part, yet it belongs strictly in the qualitative series.

Metabolic defects may be congenital and are illustrated by all dwarfed and arrested development. In some cases an entire organ may be absent, one kidney or part of one cerebral hemisphere, and to this the name *aplasia* or *agenesia* is given. Where a part has started to develop but has not attained a development proportional to other parts it is termed *hypoplasia*, and a good instance is furnished by hypoplasia of the aorta and of the lower half of the body in consequence ; a condition which is met with in certain cerebral hemorrhages in early life and points to general arterial hypoplasia as the explanation. When a part has once acquired the proportions normal for the time of life when it is studied, and then loses in size, and usually also in function, it is said to be atrophied and the process is called *atrophy*. Many cases of so-called atrophy are strictly hypoplasia, as in chlorosis associated with undeveloped genitals and the dwarfed mind and body of cretinism. Although atrophy is often observed with various forms of degeneration and may lead directly to one or the other of them, it is to be distinguished from degeneration by the fact that the latter involves cellular death in the part ; atrophy merely implies diminution in size. Atrophy often follows closely upon hypertrophy, the size which an organ may reach being apparently limited in any case, as is true of the body as a whole.

Certain forms of atrophy are normal in certain life periods, as when the thymus gland diminishes at about the tenth year, and the genital organs undergo atrophy with the decline of the sexual function. In a sense the atrophy of muscles confined in splints, and of the cerebral cortex in old age are normal from this point of view. Lack of use or diminished use, with consequent lessened blood supply, covers these cases and also the atrophy which follows nervous lesions. Atrophy again follows mechanical pressure, constriction from adhesions, and diminution of the blood supply from any cause ; certain poisons have

an atrophic effect upon certain organs. All the varieties of simple atrophy may be grouped under one of two causes, with associated lessening of function, either imperfect blood supply or imperfect use of the blood supplied.

Atrophy may involve the whole of an organ or only a part of it; in the latter case it is called *asymmetric*; the effect of the latter form is to distort the part unless the defect is made up by another tissue. Thus in atrophy of the cardiac muscle either fat or new connective tissue may replace the lost muscular elements, and in osteoporosis of bone the marrow increases in proportion as the bone substance is lost. Fatty, pigmentary and connective tissue changes are regularly found in connection with atrophy, but in the majority of instances are associated with degeneration and belong in a later paragraph.

The physical appearance of an atrophied part varies; it is usually smaller in size, it may be variously dimpled and distorted, the capsule if present is thick and opaque, connective tissue replacement makes the organ hard, dense and tough on section, fatty replacement makes it more yielding, the anemia may give it a lighter color than normal and pigment, as in brown atrophy of the heart, may darken it. The various steps in the process are, loss of fluid, hence dryness and density, decrease in size and number of cells, vacuolation of cell bodies, wasting of nuclei, accumulation of pigment, waste of high-function cells first, loss of striation in muscle, atrophy and disappearance of vessels, relative or actual fibrous increase, replacement by fat, shrinkage and cicatrization.

Local Disorders of Metabolism; Qualitative.—These may vary in two directions, including cases where *some substance is added* to a tissue, instances of matter out of place and comprising all the varieties of infiltration, and those cases where there is *tissue defect*, including the degenerations.

Infiltrations may be deposits of *normal materials* or of *pathological products*, and among the former the material may be either *inorganic* or *organic*.

Certain trades are carried on in circumstances favorable to the ingestion of foreign bodies in a state of fine subdivision, the favorite seat of deposit in the body being the lung. Probably the dust or other matter is deposited on some part of the bronchial mucous membrane, absorbed by phagocytes and laid away in the tissue framework of the organ or in the lymph node corresponding to the site of deposit. In this way large portions of the lung are colored black by coal dust, a condition known as *anthracosis* and met with in the lungs and bronchial nodes of every dweller in cities and worker in coal. Should the amount of matter thus introduced become excessive, beyond the ability of the tissue to suffer its presence, a peculiar form of pneumonia is apt to develop, known as *anthracotic* or *miner's pneumonia*. Should a lymph node which is loaded with the foreign pigment soften and its contents enter the general circulation, the pigment may be met with in any part which eliminates or passively receives it, as in the liver, bile, alimentary mucous membrane, etc. Similar conditions occur from working in stone dust, steel-sharpening works, etc., producing *siderosis*, *knife grinder's phthisis*, *chalicosis*, and *lithosis*. Organic dust may be inhaled from working with feathers, hair, shoddy, wool, and leads to lung affections sooner than in the former case. Workers in brass, zinc, arsenic, phosphorus and mercury suffer from constitutional symptoms peculiar to the metal used, but the discussion of this form belongs in the chronic poisonings.

The inorganic material does not always come from without; often it is manufactured in the body. Several forms occur. Deposit of lime salts is called *calcification*, a normal process in the cartilages with advancing age, seen especially in ribs and larynx, and an effort at repair and protection where a foreign body is shut off by incrustation or infarcts become calcareous. Other cases are the deposits of uric acid salts, the formation of calculi, "sand" in certain tumors and various concretions.

Calcification.—Though the term calcification refers to salts of lime they are not the only ones found in the tissues; beside

calcium carbonate and phosphate, oxalates are often present and the corresponding magnesium compounds. If these salts are in large amount the tissue may be solid with them and is then said to be *petrified*, as is sometimes the case with a fetus in extra-uterine pregnancy, the product being called a *lithopedion*. Two forms of calcification are found, one where the mineral matter is deposited in the tissues and another where it gathers round a nucleus in some body cavity; the latter are spoken of as *concretions* and often have various pigments and other elements included in them.

In the tissues the earthy salts are deposited in parts which are either dead or dying; even when as one of the regular changes of advancing age such deposit occurs in the arteries and elsewhere, a hyaline change in the basement substance and an atrophy of the elastic fibers has preceded it. The nutrition of the part involved is always imperfect, as is seen also in some tumors, like uterine fibromyomata, which often bear large amounts of earthy material scattered through them. Such calcification is not bone formation and must be carefully distinguished from it; the process is passive, the structure of bone is not reproduced and it occurs in a part whose nutrition is below normal. Usually the salts lie in the fibrous framework of the tissue, between the cells, but the latter may also be the seat of the deposit; in either case under the microscope we observe very fine granules in the parts mentioned, highly refractive, dark with direct illumination, which are insoluble in ether but dissolve in hydrochloric acid with the liberation of carbonic acid gas; such bodies take hematoxylin strongly. If the cells are involved the grains occur in the protoplasm and in time hide the nucleus. Such changes occur commonly about foreign bodies, and always accompany trichinæ in the muscles; other cases are in the lung apex about foci of tubercular infection, in tendons, forming "exercise bones," in ganglion cells and vascular walls in old age and in the kidney after chronic mercury poisoning. A *metastasis* is spoken of when bone is being de-

stroyed in quantity and the lime salts are laid down in distant parts. The chemistry of the process is probably a change of the soluble lactate and glycerophosphate of lime into the insoluble carbonate and phosphate and their precipitation from the blood in parts whose nutrition is impaired, because the presence of free carbonic acid is lessened in such parts.

Concretions are formed in some cavity or canal of the body about some other substance which acts as a nucleus, it may be a bit of dead tissue, thickened mucus, or a small foreign body. The chief concretions are the gall-stones and the urinary calculi, others form in the prostate about amyloid bodies, in the pancreatic and salivary ducts, in the appendix and elsewhere. The conditions favoring such formation are an abnormal composition of some excretion, chemical decomposition, the presence of a solid nucleus and something to bind together the various layers of deposit; thus, as in stone in the bladder, thickened mucus surrounds the nucleus, earthy salts are deposited in this, again a layer of mucus and a layer of mineral matter, and so on as long as the calculus remains. Gall-stones may contain also, or chiefly, cholesterin with biliary acids and pigment, and are specially liable to form on account of the high percentage of solid matter in the bile (14 per cent.) and the narrowness of the biliary passages.

Urate Deposits.—Sodium quadriurate is soluble in the blood plasma and may circulate as a waste product on its way to the kidney, but in certain constitutional conditions it is converted into the insoluble biurate and is then deposited in portions of the body which are normally of relatively low temperature, as the external ear, the small joints of the hands and feet, ligaments, tendons, etc. Such *tophi* under the skin may break through and discharge a thick whitish semi-fluid made up of mineral salts and a little plasma. In the new-born child, during the first week of life, precipitated sodium urates occur in quantity in the renal tubules and often appear in the pyramids as converging yellowish white lines which meet in the papillæ;

such *urate infarctions* are supposed to prove that a child has been born alive and are so far trustworthy that their presence justifies the belief although their absence is not a proof of still-birth.

Stones often form in the renal pelvis from calcium oxalate or urates and either remain there and increase or pass down to the bladder and form the nucleus for phosphatic calculi. Wherever concretions occur they may lie quietly for a long time without apparent damage to the container, or by irritation of the part lead to ulceration and perforation.

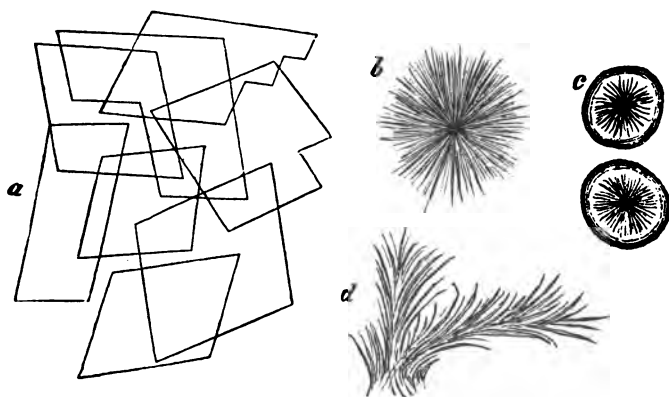
The sand in the pineal body, choroid plexus and certain tumors, as psammoma, will be treated in a later section.

Fatty Infiltration.—The essence of an infiltration is the passive accumulation of the infiltrate in the tissue, being usually brought there from a distance and consisting of normal material or of pathological products. If normally present in the part then the infiltration consists of an excess. The proper cells of the part are normal or suffer passively from the pressure of the infiltrate and consequent interference with function. Fat in and among the cells may be an *infiltration*, when more or less normally present in the part, or an *invasion* when not normally found there; an example of the former being fatty liver, and of the latter, fat between the muscle fibers of the heart. That the process is in great part a mechanical overloading and not the result of local cell destruction is proved by the persistence of the protoplasm and nucleus of the cell even when a globule of fat has pushed them far aside; if the fat is removed the cell may recover perfectly. Even when this reaches a high degree, as in the liver, the fat may be dissolved out of the cell by ether and a normally staining nucleus found; beyond a certain grade the cell contents must suffer atrophy from the pressure. In fatty degeneration the picture is a very different one. There the protoplasm is dying, it contains many fine droplets of fat, and its staining power is nearly or entirely lost.

Fatty infiltration may be the expression of excessive food, fatty and other, or of inability to use a smaller amount of nutri-

ment, or of accumulation of fat in the circulation from tissue destruction, nervous and osseous, elsewhere. The first is seen in obesity of all grades, the food taken in beyond the bodily needs being laid away in the tissues in the form of fat, and certain kinds of food and drink and an apparent bodily tendency to fat formation, aided by deficient oxygen, are often the factors, alcoholic patients, beer drinkers especially, having enormous fat accumulations in the abdominal organs and walls. In such cases the fat appears first in normal situations, under the skin, about the mammary glands, in omentum and mesentery, and in the liver; afterward there is hardly a tissue which may not be invaded. Often but one organ is involved when the case is one of inability to use the fat introduced, namely the liver, and this may be larger and heavier than normal from the fat when the general picture is one of extreme emaciation, as in tuberculosis

FIG. 7.

CHOLESTERIN PLATES, MARGARIN NEEDLES. (*Ziegler*.)

a, cholesterol plates; *b-d*, groups of free margarin needles; *c*, the same in fat cells.

and carcinoma. The explanation is in part that the liver cells can not make use of the fat brought from the alimentary canal by the portal radicles, and partly an actual increase in total amount

because these patients for months take nothing but very fatty food, eggs, milk and ol. morrhuae. In such a liver the fat is found first at the periphery of each acinus, in later stages all through it, and if there is doubt as to its nature the absence of fatty degeneration elsewhere will show that it is a high grade of infiltration; the same degree of fatty degeneration in the liver would necessitate a similar degree in other parenchymatous organs. Chlorosis and diabetes, nerve lesions with destruction of myelin, bone lesions with injury to marrow, and certain ages as puberty and senility present other instances, the last two being closely dependent upon disordered blood formation. Another form occurs as replacement for dwindling tissues, as in atrophy of the kidney and increase of its fatty capsule. Where fat accumulation has reached a marked grade small stars of margaric crystals and rhombic tables of cholesterol are found microscopically. In the gross a fatty organ is usually large, marbled and mottled if the fat is irregularly placed, yellow unless congested, less dense but heavier than normal.

Glycogen.—Infiltration of the tissues with glycogen, where not normally present, or in excess in proper sites, is purely an infiltration; conversion of cell proteid into this carbohydrate has never been observed. Liver, muscle, cartilage, embryonic and placental tissues normally contain glycogen; if found there in great excess, or in other tissues where normally absent, it appears as glistening, homogeneous granules within the cells or as balls, often concentrically marked, of more or less regular shape, in various lumina or free in the blood; the amyloid bodies found in the prostate glandules are similar bodies. In the blood of certain anemias and of diabetes, and in tumors formed in parts which in the embryo are rich in glycogen, as chondroma, perosteal sarcoma, myoma, such granules are common. On applying iodine the granule becomes brownish red, on heating or adding saliva the color is lost; amyloid keeps its brown color in the latter conditions and becomes blue on adding sulphuric acid. Glycogen derived from liver, kidney, muscle and leucocytes

(and pus) is soluble in water ; that from epithelium and cartilage less so ; it is insoluble in alcohol, convertible into sugar (maltose) by dilute acids and ferment, and when pure is an amorphous white powder. It resembles both starch and dextrin. In certain tissues it is not found pathologically, as infectious granulomata, most tumors of the histoid group.

Edematous Infiltration.—Usually when there is venous stasis or other cause which fills a part with edematous fluid, the cells escape for a time, merely pushed apart by the infiltrate or compressed by it ; but after a time, the cell body takes up the fluid, becomes distended even to bursting, and fatty or other degeneration follows. Many skin diseases associated with the production of vesicles and blebs exhibit this phenomenon, as also superficial burns, certain inflammations and beginning cloudy swelling. It is noted also in congenital edema and syphilis. It can be seen in granulating wounds treated by water-bath and in epithelia kept in the moist state.

Cholesterin.—Fatty detritus from decomposing tissue and exudate, as in sebaceous cysts, often contains thin plates of cholesterin. They are four-sided with reëntrant angles at one corner or along an edge, and may be visible as little shining specks. Cholesterin is found normally in the bile, held in solution by soaps and bile acids. It is soluble in benzol, chloroform and ether, turns red with sulphuric acid and appears in both fatty infiltration and degeneration, especially the latter.

Pigment.—In the vast majority of cases the deposit of pigment in the tissues is a passive process, a true infiltration, and its origin may be outside the body or internal. Dust inhalation has been mentioned ; tattooing is a common form of introduced pigment, and it has been claimed that workers in brass absorb metal particles through skin and hair-follicles. A better instance of foreign pigment is the condition called *argyria*, due to long use of silver, the pigment being found in the stroma of many tissues as fine brownish grains, probably silver albuminate colored by light. The skin, the alimentary mucous membrane, the

choroid plexus, and the medullary portion of the kidney are the favorite sites of deposit ; epithelia usually are free.

Of the pigments found in the body normally some are the product of cell activity and perhaps formed from albumin (this is denied by many observers), often containing nitrogen and sulphur, some are formed from the blood by the cells, and others come from destruction of the red cells, either as extravasation and hemorrhage or while still circulating. These pigments may be conveniently divided into those which contain iron and those containing none :

I. WITH IRON.

Hemosiderin.
Malarial, one form.

2. WITHOUT IRON.

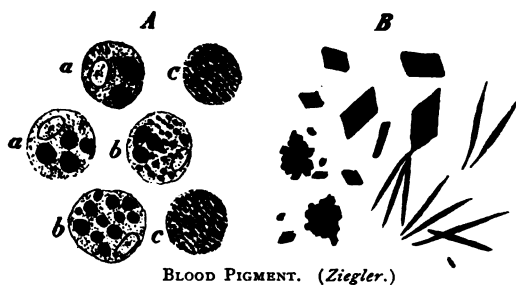
Hematoidin.
Bilirubin.
Melanin.
Malarial, one form.
Lipochrome.
Hemofuscin.
Of melanotic tumors.
Of ochronosis.

Normal sites for pigment are the rete Malpighi of the skin, the retina, fatty tissue, corpora lutea, the pia and choroid, ganglion cells, etc., and in most of these places it may appear in physiological excess as in the skin during pregnancy ; or it may appear locally as freckles, in pigmented moles and some tumors. In other places it is not made out by unaided vision, as in muscles and sweat glands. Microscopically it appears as small grains or balls, or in plates or needles and varies in color from pink and light yellow to red, brown and black. Its seat is either in cells or in the basement substances and may be limited to one kind of tissue or generalized. Special cells of the skin which carry pigment are called *chromatophores*.

Hemosiderin.—This pigment is derived from the red cells (hemoglobin, methemoglobin) whenever blood is destroyed in

circuit or outside the vessels. It occurs as yellow, orange or brown grains and differs from normal hemoglobin in its reaction to microchemical tests; treated with potassium ferrocyanide and hydrochloric acid it turns blue, with hydrogen sulphide, black. It occurs in small extravasations, thrombi, in the malarial plasmodium, and, by its destruction, free in plasma and tissues and in the liver in pernicious anemia; absorbed after hemorrhage and

FIG. 8.



BLOOD PIGMENT. (Ziegler.)

A. a, Cells containing amorphous pigment, in larger, *c*, in smaller particles. *B.* Needles and rhombic tables of hematoidin.

deposited in lymph nodes, spleen and kidney it forms blood-pigment metastases. In contact with sulphur compounds, as in suppurating wounds and after death in intestine and peritoneum, it becomes black and causes pseudomelanosis.

Hematoidin.—This derivative of blood coloring matter appears in fine granules or crystalline needles and stars; it is yellow or red, soluble in ether, chloroform, carbon bisulphide, insoluble in water and alcohol and gives no iron reactions. With sulphuric acid it gives the color play of bile pigment and chemically it is isomeric with bilirubin. In the tissues it is found in cells and outside, in the central portions of blood masses which have been extravasated and in various organs by metastasis. Both these hemoglobin derivatives are deposited in spleen, lymph nodes, kidney and liver and may be recog-

nized in the gross by the resulting gray or black hue of the organ ; they are excreted by the kidneys and the alimentary mucous membrane.

Malarial pigment is of two kinds, one identical with hemosiderin, and one free from iron which is found in the plasmodium only and whose nature is uncertain. *Lipochrome* is the yellow coloring matter of fatty tissue and of corpora lutea and chloromata. *Chloroma* is the name given to certain yellow or green sarcomas and as the pigment acts somewhat like fat it is probable that it is an altered lipochrome. *Hemofuscin* is an iron-free pigment found especially in the muscular layers of the stomach and intestine. In necropsies on the bodies of hard drinkers the pigmentation is frequently well marked in the gut. It may be due to destruction of the red cells by alcohol. General pigmentation of the body by red-cell destruction is called *hemochromatosis* and may sometimes be recognized during life. *Melanin* is a dark brown or black pigment formed in certain tumors, especially sarcomata developing in parts of the body normally containing pigment ; by metastasis of the tumor the pigment is carried to various organs. It may be derived from the blood, but has been thought to be the product of activity of the cells involved, on account of the presence of sulphur in appreciable amount. *Ochronosis* is the name given to the dark yellow or brown coloration of cartilage, tendinous insertions, atheromatous plates and lymph nodes in old persons ; the pigment is free from iron and lies diffusely in the tissues.

Discoloration of the tissues by biliary pigment is called *icterus*, and is due partly to the imbibition of dissolved bile pigment, partly to the deposit of granules, and with the latter there may be biliary acids in fine needles. Bile pigment is manufactured in the liver from the hemoglobin, its iron being disassociated, and is twofold, bilirubin, identical with hematoidin, and biliverdin, an oxidation product from the first. The liver is the only place where bile pigment is formed and hence jaundice (*icterus*), is only hepatogenous and not hematogenous ; even when poisons

circulate in the blood and disorganize it (toluylendiamin, arseniuretted hydrogen, after anesthetics and transfusion, snake bites, etc.), the icterus develops from biliary stasis. During life the icteroid hue is chiefly noticeable in the conjunctivæ, general integument, and sweat, but the pigmentation may occur anywhere except in the cerebrum, and even there in icterus of the new-born. In the urine the converted hematoidin occurs as urobilin and may be recognized by usual tests.

Cutis aenea in Addison's disease, the pigmentation with atrophy regularly observed in heart, adrenals, kidneys and testes in advanced age, and similar changes in various cachexias are instances of general impairment of bodily function and constitutional decline and are probably all connected with dyscrasia of the blood-producing organs with consequent excess of pigment in the circulation and passive deposit.

Degeneration and Necrosis.—Local disorders of metabolism involving tissue death are grouped under two main heads, degeneration and necrosis, the former including all cases involving cellular death, often but one kind of cell in a mixed tissue showing the alteration, and the latter those which involve death of the tissue in mass without distinction of kind.

THE DEGENERATIONS ARE :

Cloudy,
Fatty,
Hydropic,
Hyaline,
Mucoid,
Colloid,
Amyloid,
Bone caries.

THE NECROSES ARE :

Coagulation,
Caseous,
Liquefaction,
Fat,
Of bone,
Hemolysis,
Sphacelation,
Gangrene.

Cloudy Swelling.—This form of degeneration, also called granular or albuminous, begins as a collection of fine granules in the cell protoplasm, giving it a turbid non-translucent look, and at

the same time the cell becomes swollen, so that its normal appearance is lost ; the granules are insoluble in ether, soluble in acetic acid, and alkalies, and hence resemble albumin. Such changes are sometimes associated with inflammation and sometimes are the first stage in a fatty degeneration. In the gross an organ so affected, as the kidney, is swollen, the cut surface when released by the knife bulges up and the look of the tissue is opaque, as if cooked ; hyperemia may be present also. Microscopically the refracting granules appear, the cells are large, there may be vacuoles, the nucleus is normal or at times involved ; or the entire cell may have lost its staining powers. Cloudy swelling is common after diseases with high temperature (typhoid, variola, diphtheria) and in certain poisonings (arsenic, phosphorus, mineral acids), and from bacterial invasions. Three elements enter into the process, an imbibition of fluid, increase of supplied proteid or the conversion of the cell protoplasm into granular precipitate ; the latter source of the granules is the more probable and the process is strictly a degeneration with loss of the normal cell structure. The organs which present the change most clearly are the muscles, the liver and the kidney.

Hydropic degeneration is closely allied with the former as that is with the fatty variety. It is observed in cells which have imbibed fluid from the surrounding tissues, as in the case of epithelia, the cell contents being pushed aside and the space occupied by clear fluid so that the nucleus presents at one side like the seal on a ring, and the resemblance to plant cells is marked. In muscle the fibrillæ are pressed apart and the cut section has a finely frothy appearance ; in time the fibrils liquefy. Such hydropic changes are different from passive edema, for in the latter case the cell may lose the fluid and return to the normal, which can not happen in this form. It occurs in inflammations and tumors.

Fatty Degeneration.—Normally the fat in the body is introduced in the food and drink, and it is supposed that the body

has the power to manufacture it from vegetable fat, adipose tissue of the lower animals, starch and sugar, and also from proteids, though the details of the last source have not been worked out and its existence has been denied. It is said that a proteid may be split into two bodies by the cell, one holding nitrogen and ending in urea, the other a carbohydrate from which fat may be formed as from ingested carbohydrates; normally such fat is then oxidized and disappears. Fatty degeneration would then be persistence of fat formed at the expense of the cell protoplasm. In fatty degeneration of cells, one of the most widely distributed forms of cellular death, the change from proteid to fat is supposed to occur within and from the protoplasm of the cell. (Such a degeneration is sometimes termed "necrobiosis.") Macroscopically an organ affected with fatty degeneration may be somewhat larger than normal, but more often it is distinctly smaller, for we have to do with degeneration and atrophy and not the addition of something to an organ of normal size; this alone would serve to distinguish the condition from simple infiltration, but in addition the entire organ is usually involved, not certain zones of it, the fat is scattered throughout in smaller granules, and the same irritation or toxin which caused the change in one parenchymatous organ has produced similar changes in others. Under the microscope the fat is in fine granules and droplets, or of irregular size, invading all cells of one kind impartially, and highly refracting, soluble in ether and alcohol and stained with osmic acid and soudan III. as elsewhere. When the degeneration has attained a high degree many of the cells are broken up into detritus and the organ shrinks; epithelia, connective tissue and muscle may be affected, the heart, kidney, liver and nervous organs especially. The change is due to interference with cell nutrition; hence it follows local and general anemia, great loss of blood, various poisons as camphor, arsenic, phosphorus and some fungi, diphtheria and tuberculosis; after acute diseases with high temperature the change may be due in part to the fever and in part to the special poison of the disease.

In new growths of normal tissue or in tumors, and associated with both cloudy and hydropic degeneration, fatty changes in the cell are common. Extreme degrees of infiltration sometimes pass over into degeneration.

With the fat in the degeneration last described there may also be crystals of fatty acids, the bodily fats being combinations of glycerine with margaric, palmitic and oleic acids, and also thin rhombic plates of cholesterin; the latter is normally present in myelin, bile and the blood, and occurs at times in the urine. It is soluble in boiling alcohol and ether; with sulphuric acid it turns violet or red. It is probably an intermediate product of albumin catabolism.

Hyalin Degeneration.—As in many of the other degenerations, the name comprises more than one kind of altered proteid, and the distinction is chiefly physical and not chemical. Hyalin is clear, glassy, homogeneous and refractile; it contains nitrogen and can be turned into sugar by boiling with dilute acid, reducing then the copper in Fehling's test. It stains by the acid anilin dyes (acid fuchsin, eosin, magdala red), less by the basic and at times by fibrin stains; insoluble in water alcohol, ammonia solutions and weak acids. It does not respond to iodine. Several varieties are found, including that formed from epithelium, *keratohyalin*; that called *conjunctival* or secretory from connective tissue; *hemal* as formed in thrombi; *inflammatory* in exudates or serous membranes, in renal tubules; and the *hyalin* of *tissue necrosis* in tubercular and other coagulated areas.

The source of hyalin is cell protoplasm, especially in leucocytes from which small granules of it escape on treating with hydrochloric acid, and endothelium, and while it has been compared to proteid altered by heat as in cooking it differs from that form of coagulated albumin by its insolubility.

The site of the material is either intracellular, as in coagulation, or extracellular, extruded from the cells or coagulated from the lymph between them. It is particularly noted in con-

nection with blood-vessels, as in the walls of aneurysm, in sclerosed arteries, in endocarditis and the thickened cardiac valves, in small arteries of lymph nodes and the mucous membrane affected by diphtheria. Collections of extravasated blood often undergo hyalin degeneration; it is found on the chorionic surface of the placenta and a variety of it develops in the muscles during protracted diseases with great temperature variation, as typhoid. Blood plates and leucocytes undergo the change in some diseases and form hyalin thrombi and emboli in arterioles and capillaries; tubercular masses, gummata and certain tumors, especially endotheliomata, also become hyalin as part of a regressive change. It is often not the only form of degeneration present, being combined with fatty and calcific, closely related to fibrinous and necrotic coagulation and at times the first stage of amyloid.

In the gross there may be nothing noticeable, as the hyalin is often confined to the walls of the smaller vessels; or the part may be dense, increased slightly in volume, pale, at times containing minute vitreous scales, and if a precursor of amyloid giving the iodine reaction. In muscle the tissue is reddish yellow, semiopaque and lustrous, and friable; on mucous membranes small false membranes are found or slightly swollen submucous plaques.

Microscopically it may appear in spheres and granules, or as a homogeneous mass, the nuclei of the part staining feebly or not at all, as in cerebral membranes, plexuses and tumors and the pineal body. A granular form occurs in leucocytes, which may perhaps be regarded as monocytic glands, and from them recovered with acid as above. In vessels it appears in any of the coats and affects the smaller arteries first. There is a supposed relation between this degeneration and cells derived from the mesoderm.

Mucoid Degeneration.—The degenerated matters embraced under this head are nitrogenous, derived from albumin, swell in water and then dissolve, precipitated by alcohol and acetic acids

and not redissolved in excess of the same, soluble also in neutral salt solution, caustic alkalies and alkaline carbonate solutions; they are not diffusible, being compounds of animal gum and albumin, hence called glycoproteid; they contain nitrogen and sulphur. They fix best in corrosive sublimate solution, take hematoxylin feebly, basic stains better; thionin and toluydin blue best. With dilute acid and heat they make sugar and react to Fehling's test, except synovial mucin; paramucin reduces copper without previous boiling with acid.

Two varieties are recognized, *mucin*, from the submaxillary, intestinal glands, tendons, etc., which has the qualities given, and *pseudo-mucin* which is not precipitated with acetic acid and sometimes appears refractory to sugar tests; but this second kind includes paramucin, metamucin, and perhaps others and is merely a name for all mucin which differs from the typical form.

The normal type is found in the mucous glands, umbilical cord, bursæ, tendons and synovial membranes and is either jelly-like or stringy, translucent and viscous. Pathologically it is to be recognized in two forms, the excess accompanying inflammations of mucous surfaces, poured out of the beaker cells in unwonted volume and hence thinner than normal, or collected in a thick layer on a mucous surface chronically diseased and having no apparent inflammatory reaction under it; and in the form found in the tissues where it never appears normally, as in cartilage and bone marrow. In discharges from the genito-urinary passages the fluid sometimes contains nucleo-albumin in large amount; if this were retained it might proceed to complete mucous degeneration and points to a common source of mucin.

The site of mucous degeneration is chiefly the mesodermic basement substance between cells; it occurs in connective tissue, as cartilage and fat, in marrow, in sarcomata and cysts; in bone the calcium salts disappear first and then the mucin appears. It also occurs in masses of pus cells. In cavities it collects as a thick clear fluid, afterward thinner, or it may be mixed with pus cells and colored by blood pigment; the amount may be large,

as in the gall-bladder, and the normal epithelium atrophies from pressure.

Microscopically in mucous membranes the goblet cells are more numerous and larger than normal; in the healthy condition their function does not involve their death, in the inflamed it does; inflammatory reaction coexists in acute cases. In the tissues there is partial or complete absence of basement tissue, mast cells are at times abundant, the vessels usually escape, and there may be small cysts.

Colloid Degeneration.—In this the material strongly resembles mucin in appearance, but with alcohol and acetic acid it merely swells, resembling pseudo-mucin; it is firmer and more consistent, mucin resembling mucilage among adhesive substances and colloid resembling glue; it does not involve interstitial structures but is confined to cells. Its dryer nature is seen in its shrinking and cracking at times. Amyloid reaction not given. It takes acid stains and becomes orange red with picro-fuchsin. It may stain by Gram's and Weigert's methods.

Colloid material may form in both epithelial and connective tissue cells; normally it is found only in the thyroid. In the form of degeneration it begins as small points in the cell body, refractile and homogeneous, which increase till the entire cell is involved, the nucleus either atrophied or also turned into colloid; several of these fuse and sometimes make relatively large spheres which may be marked by radiate and concentric lines corresponding to the age of different layers and consequent shrinking in the older and dryer. Where a tissue holds many such areas they often communicate with one another in a coarsely reticular manner. It is found in long mucous glands, as in the uterus, in renal tubes, the adrenal bodies, the hypophysis, in great quantity in the hypertrophy of the thyroid gland, in the prostate at times and in many degenerated tumors.

In the gross there may be small areas like swollen sago through an organ, yellow and glue-like, with increased density of the part; single and multiple cysts may be present; some-

times there are laminated concretions. The cysts may contain blood, pus, cholesterin tables and crystals of calcium oxalate. Edema often coexists.

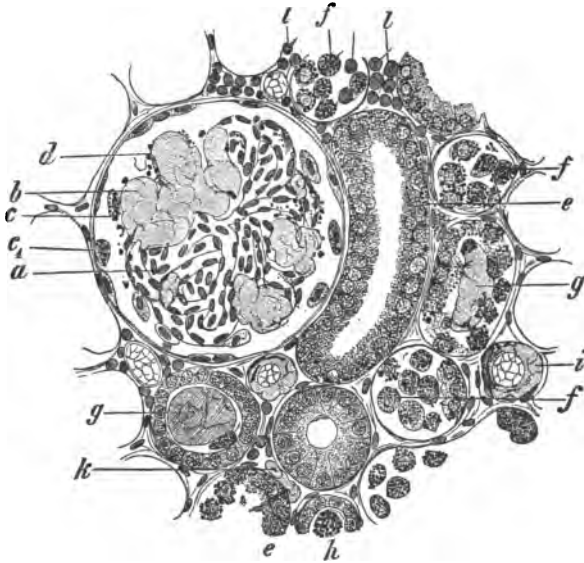
Microscopically the gland cells throughout the acini are involved, with anemia of the tissue, and the swollen part may exert pressure which atrophies other cells. The crystals and onion-like bodies are found as mentioned above.

Amyloid Degeneration.—Of the albuminous degenerations this is the most important clinically because of its effects on the general condition, although a tissue involved in any of the albuminous degenerations is probably beyond recovery; and yet it does not so often come to the notice of the pathologist in modern times because of the great advance of surgery and the infrequency of the long suppurative processes which used to be tolerated. Amyloid material is glassy, colorless or slightly yellow, firm and somewhat elastic. With iodine tincture, alone or combined with potassium iodide, it turns mahogany brown; on adding chloride of zinc solution or sulphuric acid it becomes blue to violet; with methyl violet (iodomethylaniline) it stains red, normal tissue being blue-violet. Because of the reaction with iodine amyloid obtained its name (meaning "like starch"), and was considered an animal cellulose and hence a carbohydrate; it is now known that it contains nitrogen and is albuminous, differing from albumin in its reaction and in resisting chromic acid, alkalis, alcohol and ferment action (pepsin, putrefaction); but pure and in powder, pepsin and weak hydrochloric acid digest most of it, the rest being nuclein. Trypsin digests it and sulphuric acid splits it into leucin and tyrosin.

Amyloid is therefore a degeneration product, without a type in the normal body, the result of nutritive changes in proteids. It appears in the body after chronic suppuration and diseases accompanied by it, tuberculosis of lung and bone, syphilis, ulcerating carcinoma, varicose ulcers, etc., and may occur also in chronic dysentery, leukemia, typhoid and actinomycosis; occasionally it occurs in the child without any such chronic disease

as an antecedent. In all these cases we are justified in referring the product to the unexplored territory of the pathological ferments.

FIG. 9.



AMYLOID KIDNEY. (Ziegler.)

a, normal vessels of the glomerulus; *b*, vessels which have become amyloid; *c*, *c*₁, fatty epithelia; *d*, fat lying in drops on the glomerulus; *e*, fatty epithelium in urinary tubules; *f*, the same, desquamated; *g*, hyaline cast; *h*, fatty cast; *i*, amyloid change in vessel wall; *k*, amyloid capillary; *l*, cellular infiltration of connective tissue.

Its site is frequently in the walls of arteries and capillaries, the endothelium not affected, the lumen being quite or nearly closed; usually the media and intima are the site of its appearance, less often the adventitia; it may be irregularly distributed along the course of the vessel in rings and diamond-shaped patches with wide normal intervals between. In the lymph nodes and the spleen it attacks the connective tissue and the capsule is often thickened; in the parenchymatous organs of

man it is usually confined to the interstitial structure, in some of the lower vertebrates it may involve the cells also; gland cells suffer passively or degenerate from interference with nutrition and become fatty. At times it follows hyalin change and involves the same parts.

In the gross the appearance differs according to the amount of the change and its locality; if confined to small vessels it may not be visible. Otherwise the part is swollen, dense, elastic, increased in weight, the form is not distorted, pale from its anemia, dull and glistening on section, translucent in thin section, and with a peculiar look which has given its name of "waxy" degeneration. Many organs may be involved at once, especially the liver, kidney, spleen, adrenals and colon. The question whether the amyloid is formed in the blood and deposited in the organs, that is, whether it is an infiltration, or whether it is the result of local variations in proteid metabolism, affecting many organs and seeming general at times, in other words a true degeneration, has the weight of authority for the latter. We recognize a reciprocal relation between cell activity pathologically disturbed and variations in supplied albumin, we suppose the presence of a ferment foreign to the organism, and explain the interstitial amyloid as partly an extrusion from the cells and partly a coagulation between them. The result of amyloid degeneration clinically is loss of function from local anemia and interference with the cell, general anemia and cachexia because so many of the chief organs are attacked, many of them occupied with blood formation. In the gut ulcers may form and hemorrhages occur from them. Its course is slow, usually through several months.

The microscopic appearances are implied in the above.

As a *local manifestation* amyloid occurs in granulation tissue and parts chronically inflamed, in connective tissue hyperplasia, in tumors with other degenerations and in gland lumina as concretions. On the conjunctiva it occurs with hyperplasia of adenoid elements and resembles trachoma; in the larynx it is

found in syphilitic scars, as also in lymph nodes, liver, and in tumor-like swellings under mucous membrane. In these cases it occurs in the basement substance, at times with hyalin material, and gives the iodine reaction.

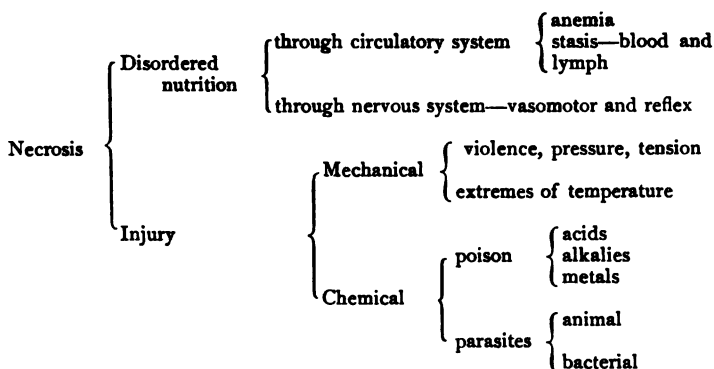
Corpora Amylacea.—Through the accident of a name these bodies have been supposed to be amyloid; both take their name from starch (amyl), but the degenerated material does so because of its chemical reaction and the concretion because of its concentric or eccentric markings like those on a starch granule seen under the microscope. Corpora amylacea come from the most varied sources and both normal and pathological conditions, and undoubtedly the term includes many different forms; their origin and chemical nature have not been entirely determined. They are small ovoid or spherical bodies, at times visible to the naked eye as brown grains (prostate), do not swell in boiling water, split with dilute acid or melt in fuming nitric. Microscopically they are homogeneous if young, marked by concentric or radiate lines if older, made up of a central darker portion at times consisting of several smaller ones, which alone may be marked, and a lighter or yellowish outer zone; with iodine they may become red, or, even without sulphuric acid, turn blue or violet at once; sometimes only the central portion reacts. As they are a regular phenomenon in the degenerations of old age, it is reasonable to consider them a degenerative product everywhere; they contain phosphorus and nitrogen and seem related to lecithin. They may form from epithelium, as in prostatic lumina, or from connective tissue as in fibroma of the dura. They have been recognized in the following also: spinal cord, ependyma of ventricles, lung, inflamed areas, in bile and phleboliths, and in certain tumors as carcinoma.

Caries of Teeth and Bone.—Although quite different from the degenerations already described, yet as the only molecular death which osseous tissue can suffer caries belongs in this group; it will be treated at length in the division of Special Pathology, Part II. In caries the bone cells become fatty or gran-

ular, the basement substance is absorbed or degenerated into mere detritus, or the lime salts are extruded and the basement substance becomes fibrillary and atypical and undergoes fatty degeneration. Suppuration is commonly associated with the caries.

The Necroses.—Distinguished from death of the individual cell, singly or in groups, or of the basement membrane, neither of which may destroy the function of the part at first, and from which it is possible for an organ to recover if the process can be arrested or ceases of itself, we have the various forms of necrosis, which stop function at once and permanently and from which there is no recovery for the part, though the organism as a whole may slough off the diseased portion or wall it in by fibrous tissue and lime incrustation.

The distinction is partly one of degree, necrosis being always a worse condition for the part, destroying it totally, than degeneration of one of its elements. It is partly also a distinction in kind, for although degeneration often leads to necrosis and is combined with it, yet certain forms of necrosis are clearly separated from other pathological processes. The name is applied to massive death of normal tissues and similar changes in neoplasms and inflammatory products. If grouped according to cause we have two main divisions, those due to disordered cell nutrition and those due to injury, and the results vary according to the patient's age, health and ability to resist disease, the integrity of the blood circulation in the part and hence its temperature, the condition of the lymph stream, the activity of the cause and the duration of its influence, the presence of other diseases and idiosyncrasy. The following scheme of the causes will make the subject clear :



It is perhaps seldom that one cause acts alone ; commonly two or more act together or one acts in more than one way, and the whole is accompanied by infiltration, degeneration or both ; in other words the condition is very complicated and the descriptions and subdivisions on paper are a device toward comprehension.

The various tissues are not equally susceptible to the causes of necrosis ; as a rule the more highly specialized are destroyed first, and a rough scale may be given thus, the less sensitive last—gray nervous tissue, white ditto, gland cells as kidney and liver, epithelium, muscle cells, blood-vessels, connective tissues. The result of necrosis is removal of the part either by absorption, or if on a surface, sloughing, partial replacement by scar tissue, or failure of such repair and ulceration remaining, partial separation from the body as sequestrum, encapsulation and cyst formation.

A good example of necrosis from anemia is found in the production of an infarct from embolism, the part deprived of its nutrition at once becomes anemic and dies. More gradual change of similar nature is seen in gangrene of old age, the diminished lumen of the arteries with weakened heart action slowly depriving the part and setting up dry gangrene (mummification) of the foot. Inflammatory exudation, as between periosteum and

bone, may cut off the nutrition and set up necrosis. When the venous return of a part is stopped, as in hernia incarcerated by a tight ring, it suffers passive congestion from which it is possible to liberate it for a time ; after that death follows inevitably as local gangrene. Mechanical influence, crushing and similar injury, acts partly in complete destruction of the cells at once, and partly such injury to the vessels of the region that nutrition cannot continue ; as lighter grades of the same thing may cause inflammation, we often find necrosis and inflammation in different areas of the same organ, and in the effort to remove a necrosed portion, inflammation is one of the chief factors. Heat and cold if extreme kill the tissues at once, and usually those which lie at a distance from the heart and have relatively little blood. When foreign bodies distend the wall of the canal in which they lie, this is also a case of interference with nutrition and may lead to perforation, as in biliary calculi. In connection with this there may be other influences, as when gases and bacteria from the intestine join with foreign bodies in some part to weaken and perforate the wall. Corrosive poisons act either by destruction of the part touched, removing its water and making new combinations with its elements, or by destroying the circulation ; and perhaps the action of bacterial toxins, as in diphtheria, is partly of the same nature. Some infections constantly invade new territory, with increase in the number of the germs and of their products, and thus a gangrenous process migrates ; in some cases gas is produced in quantity in the tissues (as from *bac. aërogenes capsulatus*) and local emphysema results, its pressure and the nature of the gas aiding in the death of more tissue. Necrotic processes may pass from place to place interruptedly, as when a middle ear suppuration causes septic thrombosis of a cerebral sinus and an embolus from here sets up gangrene of the lung. Necrosis, sepsis and inflammation are closely related.

Microscopically the cells in a necrosed part remain as ghosts which do not take stains, or are destroyed beyond recognition. The cell body loses its normal granulation, becomes cloudy, its

protoplasm breaks up, vacuoles form, hyalin changes may occur ; if in lymph, edema sets in and the capsular membrane may burst and set the altered elements free. The nucleus may merely lose its staining power or break up (karyorhexis), or its chromatin may be altered and in part removed from the nucleus (karyolysis), and cell and nucleus dry up to an indifferent scale ; in these changes the flowing of the lymph stream through the cell is supposed to play an important part, the cell elements being passive. The basement substances are variously degenerated and liquefied, contained lime salts, as in bone, being reduced to little collections of mineral grains or dissolved and removed.

The various kinds of necrosis (grouped mainly according to gross appearance) are :

Coagulation necrosis,
Caseous necrosis,
Liquefaction necrosis,
Of fat tissue,
Of bone tissue,
Of blood,
Hemolysis,
Gangrene.

Coagulation Necrosis.—When a part is dead or dying and is still bathed in tissue lymph, this fluid may coagulate either between the cells or within them ; if outside the cell there is coagulation within and about the blood-vessels, inflammatory and other ex- and transudates, and this may be observed on surfaces, as mucous and serous, or in the tissues, the result being fibrillar or hyalin or granular coagula. In the cells the nuclei are lost, the body is granular or hyalin, and after a time the cell breaks up into detritus and is removed. This form results from embolism and thrombosis, from the effect of pus, tubercle and diphtheria organisms, and from high temperatures ; certain chemicals coagulate the proteids in the tissues, as carbolic acid, leaving them firm and rigid. The part may become caseous,

cast off or dissolved by suppuration, or enclosed by fibrous tissue and the latter infiltrated with earthy salts. In the gross the part may be firm, larger, gray or yellowish. Microscopically the nuclei may retain a slight degree of staining power or none. Weigert's fibrin stain shows fibrils and grains of fibrin; all elements are involved including pus and red cells. It is closely related to fibrin coagulation though at times the fibrillæ do not take stains.

Caseous Degeneration.—This is but a variety of the first kind, but it occurs so frequently in tubercular disease that it may be mentioned specially. The coagulated area is yellowish, dry and firm, a large element of fatty degeneration associated; or it is of lighter hue, softer and creamy in consistence. It may occur in syphilis and in tumors. The degenerated cells and fibers, often mixed with fibrin bundles, take up fluid and become more or less liquefied, and may then be absorbed; or drying proceeds, lime salts deposit and a fibrous capsule forms; such areas are common in the lung where they are called areas of "healed," or better, latent tubercle.

Liquefaction Necrosis.—Where a part is not well supplied with coagulable albumins, but is bathed in fluid, necrosis occurs as a quasi-digestion of the elements and the result is a fluid holding cell detritus in suspension and variously colored by biliary or blood pigment; if later there is an addition of proteid from blood or lymph, the process passes over into coagulation necrosis, just as that form may liquefy, and the probable presence of ferments in the part makes the resemblance to digestion very close. Such areas are frequent in the brain and the cord and are known from their color as red, yellow (fatty) and other softenings; in old and partly absorbed cases the color is deep yellow or ochreous. Other cases are stomach digestion of a coagulated area and resulting ulcer, burns with blebs and vesicles where the cells necrosed by heat are digested in the fluid; and in the secondary form in inflammatory products, caseous areas, tumors, etc.

Fat Necrosis.—This form occurs in the fatty and other tissues of the abdomen, usually about the pancreas, and may be traced to the escape of pancreatic fluid, usually by transudation, when the normal flow of the secretion into the intestine is hindered. Thus when the pancreatic duct opens by its own papilla (duct of Santorini), apart from the common bile duct, a calculus lodging in the ampulla could produce only biliary stasis. When the two ducts open in common, inflammatory swelling of the papilla, calculi in its lumen, and perhaps other mechanical conditions may produce pancreatic stasis; the fluid transudes from the ducts, possibly also from the acini, into the surrounding tissue, either as a whole or in part. The fat-splitting ferment, steapsin, thus attacks the peri-pancreatic fat, and in early cases the change will be found there only. Later the fat in more distant situations is attacked and also the pancreatic tissue and vessels. A small piece of fat from any source nearly resembling human fat, stroked with a piece of fresh and nearly normal human pancreas, and kept in a moist chamber at body heat, will show similar fat necrosis after twelve to twenty-four hours. (See Pancreas, Vol. II.)

As found in the cadaver the tissue affected with fat necrosis is speckled with small, grayish points, about one or two millimeters in diameter, or they may be microscopic, which do not pierce the tissue very far in most cases and which may feel rough on palpation. Under the microscope these areas are necrotic, sometimes contain crystals of fatty acids, sometimes combinations with lime which stain intensely with hematoxylin. There is often active inflammatory reaction about. If the process persists and invades the blood-vessels death may follow from hemorrhage, behind the peritoneum or into its cavity.

Necrosis of Bone.—When the nutrition of a bone is interrupted by embolism, by stripping off of periosteum, or by the effect of chemicals, especially phosphorus, a larger or smaller mass of it dies and the process is called necrosis. The dead portion is separated from the healthy by a line of demarcation, and ex-

truded or retained in apposition ; the dead piece, called the *sequestrum*, is variously eroded by the tissue juices and may be internal or external to the bone, usually external and in bones of the limbs. In other words, this is a form of gangrene and differs from that of soft parts because of the peculiar nature of the tissue.

Hemolysis.—Various chemicals, as carbon monoxide, hydrocyanic acid and its salts, and hydrogen sulphide stop the chief function of the red cells, oxygenation, and thus may be said to cause their death ; the blood being regarded as a tissue rich in cells whose interstitial substance is fluid in health, and which is all the more complicated because containing both nutriment for other tissues and products of waste. Other poisons destroy the red cell and liberate its coloring matter, causing methemoglobinemia, as ozone, chlorates, pyrogallie acid, acetanilid, and many others. In malaria, relapsing fever and some other diseases similar effects are seen. As a marked degree means death of the patient it differs from other necroses, but the cells, both white and red, and the plasma, are altered and functionless, dead in other words, and strictly the case may be an example of necrosis.

Gangrene—Necrosis with Putrefaction.—Any necrosed area by the entrance of saprophytic bacteria may begin to undergo the process of proteid decay, the continuous chemical decompositions and rearrangements which soften and finally liquefy the tissues, with the production of gases, and resulting water, carbonic acid gas and ammonia as the end products. In the course of the process many nitrogenous compounds are formed which resemble alkaloids and are highly poisonous to the organism. The microörganisms are many, from fungi to spirilla, and succeed each other in groups after a fairly regular order, but usually there are those present which produce gas.

Gangrene occurs in two chief forms, moist and dry, the former where the tissues are still supplied with lymph and the latter where they simply mummify ; in the former emphysema is more

common than in the latter. A small portion of another and larger part, if gangrenous, is called a *sphacelus*. Where either form occurs in the old from weak heart and diseased arteries it is called *senile gangrene*; where no cause can be discovered but eating rye flour which has been spoiled by *claviceps purpurea* (the source of ergot), it is called *raphania* and frequently has broken out in epidemic form. *Toxic* and *infectious* gangrene are terms which explain themselves. *Neuropathic* gangrene is partly the result of disordered nutrition, as from pressure over a bony prominence, and partly the result of disordered innervation; this occurs most commonly as *bed-sores*. Other examples may be found in *perforating ulcer* as occurring in disease of the cord, *symmetrical gangrene* (Raynaud's disease) of distal portions of the body, fingers, toes and ears, *joint lesions* in locomotor ataxia, etc., where blood supply is probably also a factor. Beside the local process in gangrene the absorption of nitrogenous products (ptomaines) and entrance of bacteria into the general circulation are of great clinical importance.

APPENDIX TO CHAPTER V. DEATH: POST MORTEM CHANGES.

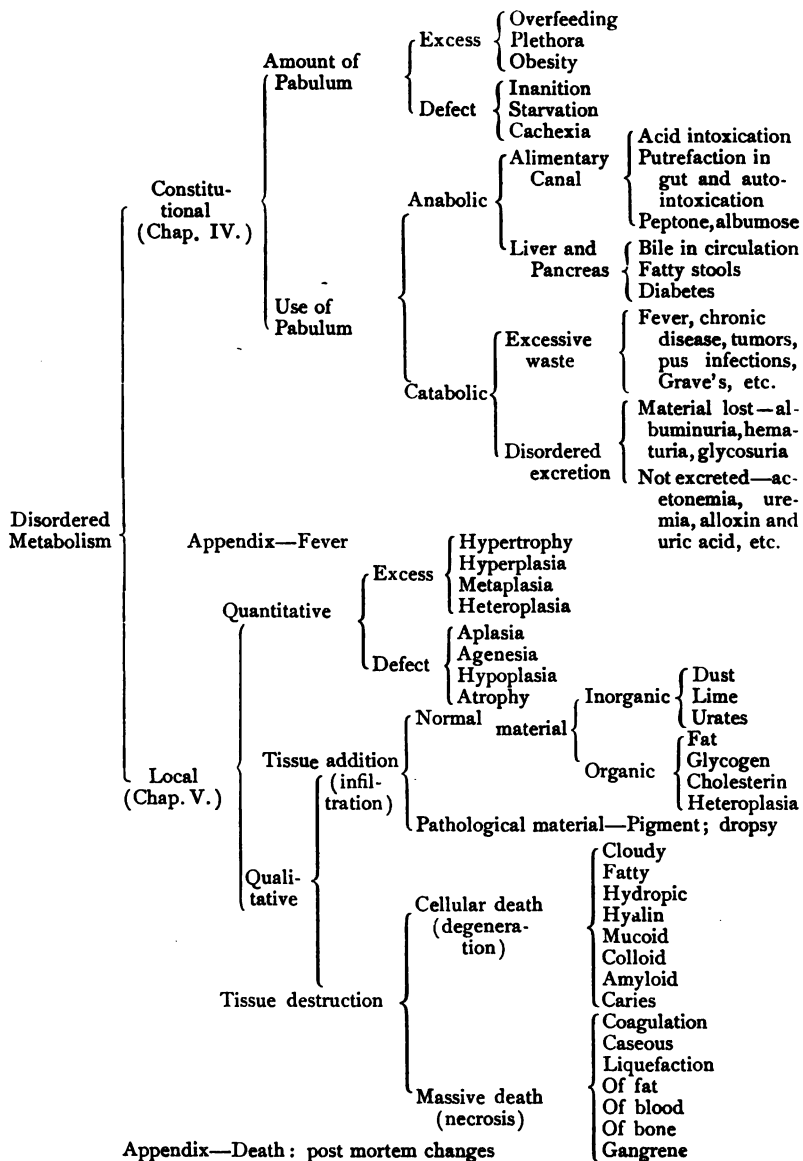
The definition of death must be so broad as to apply to all living things, and, as the essential thing in life is function, it must refer to that; anatomical, that is, structural changes follow, or if they precede are not fatal till function ceases; as when both lungs are nearly solid from lobar pneumonia and the patient breathes with only a small part of one, he is still alive until the function of respiration stops and the anatomical condition may even be on the road to recovery. Hence death is that condition of an organism in which further metabolism is impossible. The three essential functions are respiration, circulation and innervation; other functions however important may, and normally do pass through periods of quiet, these three never pause during life; respiration may be reduced to one or two a minute, as in opium coma, circulation may fall to thirty-five heart beats or less a minute, and innervation be so disordered

that the other two are irregular, intermittent and too feeble to be discerned, but metabolism goes on, no matter how little, and while that is possible there is no death. When the boundary is passed beyond which metabolism cannot be reawakened, at that instant death occurs, but in the majority of cases it is impossible to say at what second this happens. Death may occur at an advanced age through apparent failure of all the bodily powers, and statistically this accounts for about 6-8 deaths per thousand living. At any other time of life we require an explanation of the cause or at least the manner of the death, and the causes of disease already given are also causes for some deaths. Obviously an organ which has had to work harder than normal, as the heart in chronic cardiac disease, reaches a condition of senility before other organs and is exhausted before general old age; and a tissue which has suffered from a chronic disease will be less resistant to another, so a lung in tuberculosis is easily affected by lobar pneumonia. Or the destruction of tissue may not leave enough for normal function, as when a kidney is atrophied by the pressure of hydronephrosis. In many cases death is clearly secondary, as in the kidney cited, where destruction implies retained excreta and uremic poisoning, or when several diseases coexist and it requires trained judgment to decide which lesion was fatal. Death may be sudden after injury, loss of blood, severe mental shock, or when the body is overwhelmed by poison, as in carbolic acid poisoning and fulgurating cholera; or it may be protracted through a series of years, as in locomotor ataxia, part after part becoming useless and function after function lost, till disease involves function essential to life and life ends. The function and organs of locomotion and reproduction may be lost without danger to life, as also the special senses; intestinal and hepatic function may be stopped for several days and still death is not inevitable; renal function may cease for many hours; but the patient dies from failure of respiration, stoppage of the heart or lost innervation.

The appearance of the dead body varies according to its blood content, the length of time dead, the cause of the death, and the temperature of the surrounding medium. After great hemorrhage the surface is pale; if the blood is present it settles to dependent portions (*hypostatic congestion*), as the back, the lowest parts of the lungs, the spinal canal and back of the skull; if the body has lain prone corresponding lividity of the anterior half is noted. The blood is still in the vessels, for wherever pressure has been exerted it is mechanically squeezed along, leaving anemic areas. It gathers especially in venous radicles and remains fluid. The little that persists in the larger vessels tends to clot. The post mortem lividity is cherry red in poisoning by carbon monoxide. After death the bodily temperature may rise for a few hours, perhaps explained by terminal infection and great bacterial activity, but usually it begins to fall at once and loses about one degree an hour till the surrounding temperature is reached. The skin loses its elasticity and tension and where pressure has acted the body is flattened; if hyperemic before death the skin may not be so afterward, and thus most skin eruptions disappear post mortem. Where the skin has been rubbed and the epidermis removed the area becomes dry, hard, semi-transparent, and looks as if varnished; the conjunctiva also dries and becomes darker and the eye-balls lose their tension. The albumin of the muscles coagulates (formation of myosinogen within the sarcolemma; then myosin and muscle serum), it becomes acid (formation of sarcolactic acid), gives off carbonic acid and is shortened and diminished in volume and friable. The beginning of these changes is accompanied by rigidity, *rigor mortis*, which begins at once or a few hours after death in the intrinsic eye muscles, then the jaw and neck, upper extremity and thorax, abdomen and lower extremity, lasts a few hours to days and passes off as it began. If developed slowly it usually lasts longer. Smooth muscle is affected as well as striated, hence cutis anserina from rigid arrectores pilorum. After a longer time the superficial veins are marked

out as a wide, dark red meshwork from imbibition of blood coloring matter; putrefaction has begun where sulphur compounds (H_2S , PH_3) and bacteria are found, as in cecum and ascending colon, and the action of the sulphur on the hemosiderin makes sulphid of iron; as this is black and is seen through the yellow skin the effect is greenness of the abdomen. Putrefactive odors are present and the contents of the alimentary canal are pushed out by the forming gas, into the trachea, out of the mouth as a dark froth and out of the rectum. The tissues soften, epithelial and glandular first, connective last; fat from the liver may be driven up into the lung, as also clots from the right side of the heart, by the pressure of the gases; superficial parts become swollen, black or green, emphysematous, hair and nails fall off. Warmth and moisture favor the rapidity of the changes, and they occur quickly in the obese and in infants, after the puerperal state and infectious disease; cold, leanness, poisoning by alcohol and arsenic, etc., retard them.

Apparent death occurs when metabolism is reduced to its lowest terms and it may be a matter for careful investigation to determine if circulation and heart beat, respiration, and innervation even in the deepest reflexes, have disappeared; in doubtful cases the body should be kept till positive evidences of putrefaction appear, and of course without embalming or other preservative measure. Apparent death may occur in catalepsy, cholera, electric discharges, hysteria, asphyxia, submersion and after exposure to cold. The usual tests are—ligature round finger, notice if swelling occurs distally, or blood flows from a puncture; mirror held to lips, collects moisture if respiration present; tissues illuminated, as the fingers held together and a strong light back of them, reddish look if blood present, pale if absent; electric discharge to excite reflexes; X-ray examination of heart and lungs to detect movement.



CHAPTER VI.

INFLAMMATION AND REPAIR.

Definition.—Inflammation may be conveniently, though roughly, defined as “reaction to injury.”

Etiology.—The variety of factors concerned in inflammation is very great. The principal exciting causes are Mechanical, Thermal, Electrical (X-ray), Chemical and Bacterial. While all but the last of these causes frequently act in pure form, exciting various grades of inflammation in direct proportion to the quantity of the agent present, bacteria seldom figure alone as a cause of inflammatory reaction. The mere presence of bacteria is usually not sufficient to excite inflammation of a superficial tissue; there must usually be also secondary contributing causes, such as a wound or exposure to cold, and also a predisposition on the part of the individual. In the etiology of bacterial disease, therefore, are commonly associated (1) **exciting**, (2) **contributing** and (3) **predisposing factors**. (*Illus. Tuberculosis in different individuals, pneumonia in different seasons and races.*) Even with the simpler chemical agents, contributing and predisposing factors are often of great importance in determining the grade of inflammation. (*Illus. Strawberries, Lobsters, Gout and Tuberculosis.*)

The accurate estimate of the relative importance of exciting and contributing causes of inflammation is often an extremely important and difficult question. (*Illus. Development of infectious diseases in general. Relation to immunity.*) The grade and character of the inflammation excited by various agencies are usually of somewhat definite type. (*Burns, X-ray, Tubercle bacillus.*) It is an important fact that the first five of the etio-

logical agents mentioned, when acting alone, while sometimes capable of producing inflammation of purulent grade, yet are usually followed by much less intense grades of reaction, and that the vast majority of purulent inflammations are of bacterial origin. All pathogenic bacteria may, but many seldom do, excite purulent inflammation. A purulent inflammation is almost never of purely tuberculous origin.

In general bacteria excite purulent inflammations with self-perpetuating tendencies, while other agents induce non-purulent processes of self-limiting type. (*Pneumonia, Burns.*)

The Action of Bacteria in Inflammation.

Mode of Entrance.—Bacteria usually enter the body and reach a position where they are capable of inducing disease, through passages lined by mucous membrane (respiratory, gastro-intestinal, genito-urinary). Previous inflammation of these mucous passages, or other form of lowered vitality, very greatly favor and are often essential to the further development of the inspired or ingested microorganisms. Through fresh wounds which may be of very minute size, pathogenic and non-pathogenic bacteria often penetrate the tissues, and finding conditions favorable to their development, the former go on to induce infectious processes of varying extent.

In any case, the entrance of bacteria and their further development is often greatly favored by their association with various chemical poisons which are capable of causing degeneration, and necrosis, of lining cells. (*Leucomaines, Toxines.*)

The intact skin is sometimes penetrated through hair-follicles and sebaceous glands (*sycosis*), and some infectious agents are inoculated through the skin by the bites of insects. (*Mosquitoes—malaria, Texas cattle fever.*)

When infection of the blood or internal viscera occurs in the absence of any wound or abrasion of mucous or cutaneous surfaces, by bacteria which ordinarily require such aids to their entrance, the infection is said to be cryptogenic.

Mode of Action.—Once within the body, in mucous passages, in serous cavities, or in tissue spaces, their pathogenic action depends almost entirely upon the effects of poisonous principles elaborated by the bacteria, and only to a very slight extent, usually, upon the mechanical effects of their presence.

These poisonous principles are of variable chemical nature, and are produced under varying conditions. They have been classed as follows :

Ptomaines and Leucomaines are crystallizable alkaloids produced from tissue-albumins by the action upon them of bacterial growth.

1. **Ptomaines** are alkaloids developed by non-pathogenic bacteria growing in dead animal matter. (*Poisoning by decayed meat.*) They occur under some very peculiar conditions and their presence in decayed flesh is often transitory.

2. **Leucomaines** are alkaloids developed by pathogenic bacteria growing in living tissues.

3. **Toxines** are poisonous products developed from tissue albumins by the growth of pathogenic bacteria, which do not form salts with acids as do ptomaines and leucomaines, and are not crystallizable.

4. **Toxalbumins** are poisonous principles thrown off from the bodies of pathogenic bacteria. These are usually specific substances, more or less peculiar to each bacterial species, and not only are developed in the living animal tissues but have been produced by cultures of bacteria in non-albuminous media.

Toxalbumins lose much or all of their toxic properties when heated for one hour at 58° C. They do not induce toxic symptoms immediately after injection into the animal organism, but require hours or even days before giving rise to local or constitutional disturbance. They are extremely active in very minute quantities. These three facts favor the view that the specific poisonous substances thrown off from bacterial bodies are enzymes or ferments, but the present knowledge does not warrant a positive opinion on this subject.

While ptomaines, leucomaines and toxines, when injected into the animal organism, induce symptoms which often have little resemblance to the clinical disease set up by the bacterium growing in the living tissues, toxalbumins, on the other hand, usually initiate a train of symptoms which closely resembles the clinical disease excited by each particular bacterium.

Bacterial inflammations are excited then by the effects upon tissue cells of the various poisonous principles, which by chemical action cause degenerative changes and the subsequent train of vascular and cellular processes. Comparatively little importance can be attached to the withdrawal of nourishment from local infected tissues to the growing bacteria. Constitutional symptoms are produced by the absorption of poisonous products by the blood current and their distribution throughout the system. (Toxemia.)

In very susceptible individuals infected by virulent bacteria, the blood stream may be invaded, temporarily and producing distant metastatic foci of inflammation, or permanently and developing a general infection of the blood, or bacteremia.

Intoxication.—When considerable quantities of ptomaines or leucomaines or of toxines and toxalbumins are ingested and absorbed, profound constitutional disturbance may result immediately without the further development of bacteria. Such a process is called intoxication.

Infection.—When the progressive development of bacteria in the body is required before sufficient toxic material is present to produce symptoms, the process constitutes an infection.

Simultaneous development of two or more pathogenic microorganisms is called mixed infection.

Certain pathogenic bacteria excite a local inflammation which occasionally offers a ready point of entrance for a second more virulent microorganism and the new germ begins at once to dominate the inflammatory process. Such an event is called secondary infection.

THE INFLAMMATORY PROCESS.

The phenomena comprised in the inflammatory process are :

Degeneration of tissue cells (initial injury).

Changes in the circulation.

Exudation.

Secondary degeneration and death of tissue.

Growth of new tissue.

These phenomena occur in a great variety of combinations but the predominance of one or other of them usually gives a character to the process on which the nomenclature of inflammation is based. Each of them requires consideration in detail.

Initial Injury.

An **initial injury** or degeneration of tissue cells appears to be an essential preliminary to all inflammatory processes. Mechanical injury may merely divide these cells in two ; heat, the X-ray, chemical agents, and bacteria may cause very slight or very great alteration in the life processes of the cells, but in every instance some grade of injury or irritation of tissue cells appears to precede the more readily recognizable changes of inflammation. The exact character of the changes in tissue cells resulting from the initial injury is very imperfectly understood since they are of very delicate nature and are rapidly obscured by other processes, chiefly by disturbances in the blood-vessels.

Reaction to Irritation Among Protozoa.

Very pure illustrations of cellular reaction toward irritating substances are found in the behavior of amebæ and various protozoa toward foreign bodies. (*Digestive vacuoles of Ameba.*)

Observations on a multicellular myxomycete *Æthaliium septicum*, and on the *plasmodium* of *Fuligo* have brought to light the existence in these low organisms of a peculiar susceptibility towards certain influences which is known as chemotaxis.

Æthelium septicum is a multicellular ameboid organism which when placed on a moistened surface near a drop of infusion of oak-bark moves actively toward and into the infusion. The *plasmodium fuligo* is another unicellular ameboid organism which when placed on a moistened surface near a drop of one-per-cent. solution of salt, at first moves away from the solution, but later, especially if needing water, it will approach and finally enter the solution.

These observations illustrate positive and negative chemotaxis and the transformation of negative into positive chemotaxis by a process of adaptation. Similar observations may be made in human pathology; thus the tubercle bacillus is not positively chemotactic to pus cells (polymorphonuclear leucocytes), the colon bacillus is.

Reaction to Injury Among Metazoa.

In the metazoa the cells are differentiated into three layers, an outer ectoderm, an inner endoderm, and a middle mesoderm. In the lowest metazoa (*e. g.*, *Astropecten*) the mesoderm is composed largely of wandering ameboid cells. In these organisms, possessing no vascular or nervous system, the reaction to injury is chiefly confined to the wandering cells which englobe and digest or expel foreign bodies which have penetrated the ectoderm of the animal. Among these lower metazoa also are seen some of the best examples of a remarkable power of regeneration exhibited by injured cells. (*Reproduction of claws in Crustaceans.*)

Among the higher metazoa, as man, the cellular reaction to injury is best seen in non-vascular regions such as the cornea. The reaction in the cornea may rarely be limited to swelling and multiplication of the corneal corpuscles, which replace those destroyed by such irritants as zinc chloride, without the intervention of wandering cells or the appearance of vascular changes. Usually, however, many wandering cells gather through the lymph spaces to the site of the injury, where they remove foreign matter and protect the regenerating corneal corpuscles. Even then the reaction to the injury may be limited to the cells and no vascular disturbance is present.

The phenomena of inflammation thus far considered include therefore merely the (1) accumulation of wandering cells, leucocytes, and the (2) proliferation of fixed tissue cells. In all the more intense grades of inflammation in vertebrates these same cellular changes are present even to an increased extent, but their presence is usually obscured by more prominent vascular disturbances.

Inflammatory Reaction in Vascular Tissues.

1. Very Slight Vascular Disturbance. (Primary Union.)

—It is theoretically possible that the reaction from a clean incision of vascular tissue and its repair may be limited almost entirely to the fixed cells of the tissues, and some experimenters claim to have observed very pure illustrations of this fact. In such cases the incision divides the cuticle, the connective tissues, and the small vessels. If the edges of such a wound be promptly apposed the hemorrhage is slight, the ends of the vessels are promptly closed by coagula, very few tissue cells are destroyed and a slight fibrinous coagulum glues the surfaces together, so that at the end of an hour the wound appears closed and only a slight reddening about the incision indicates the moderate hyperemia of the blood-vessels. Into the coagulum the fixed connective tissue cells, irritated, send long processes, and new cells appear by multiplication of the old. The edges of the wound become more firmly united by these new cells and processes. The coagulum itself becomes condensed and fibrillated, presenting the characters of young connective tissue after the lapse of 48 hours. New capillaries are formed by the proliferation of the endothelial cells of adjoining vessels. Throughout the process very little exudation from the vessels and very few leucocytes are observed in sections of the tissues and the process is almost entirely limited to the fixed cells of the injured part. The most successful cases of primary union of surgical wounds follow some such course of repair, but in the vast majority of instances, even of rapid primary union, sections through the line of incision

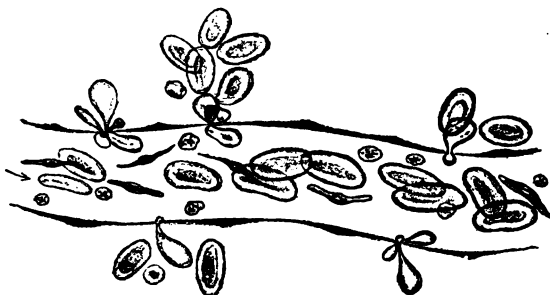
will show some dead tissue-cells, a considerable number of leucocytes, and some exudation from the blood-vessels.

2. **Marked Vascular Reaction. (Secondary Union.) Exudative Inflammation.**—The more extensive vascular changes which characterize inflammatory reaction have been most completely studied in clean wounds of the web of the frog's foot.

The injury causes, first, probably through the vasomotor mechanism, a dilation of the capillaries of the part, and increased flow of blood which continues for about an hour. Then follows a stage of slowing of the blood current and certain peculiar changes in the disposition of the blood cells and plasma.

The leucocytes increase in number, they gather along the endothelial walls of the vessels, adhere to the swollen sticky endothelium, and by virtue largely of their ameboid properties they push their way through or between the endothelial cells out into the surrounding tissues, and especially to the surface of the wound. This process is called emigration of leucocytes.

FIG. 10.



DELAYED BLOOD STREAM, DIAPEDESIS. (*Stengel.*)
Capillary of frog's tongue. (Red cells nucleated in the frog.)

Through the openings loosened by the passage of white cells, or more often through ruptures in the endothelial wall, aided by increased blood-pressure, red cells also pass out of the vessels, the process being called diapedesis of red cells. This process is more common in severe bacterial inflammations.

Exudation of blood-serum accompanies or rather precedes emigration and diapedesis. Through the swollen and more permeable endothelial cells the fluids of the blood, under increased pressure, are forced through the vessel walls to infiltrate the supporting tissues or appear on the surface of the wound. There is evidence also that the altered endothelial cells to some extent exert a true secretory action in discharging the blood-plasma. All the three above processes tend to obscure the purely cellular reaction which is nevertheless present and becomes apparent in the process of repair. After the vascular disturbance has somewhat subsided the proliferation of connective tissue cells, the budding of new capillaries from the adjoining small vessels, and the condensation of the new intracellular substance, may be seen in sections of wounds which are undergoing repair.

The above course of events is seen in surgical wounds which heal by secondary union in which the abundant exudate prevents immediate cohesion of the divided surfaces and healing begins only after the exudation has partly subsided, and usually progresses from the bottom of the wound upward. In some cases in which exudation rapidly subsides, as it should do in all aseptic surgical wounds, secondary cohesion of divided surfaces may occur, and healing occurs after a variable period as in "primary union." If the cut surfaces are permanently held apart no cohesion can occur, and healing takes place by a slower process called granulation which is best seen after suppurative inflammation.

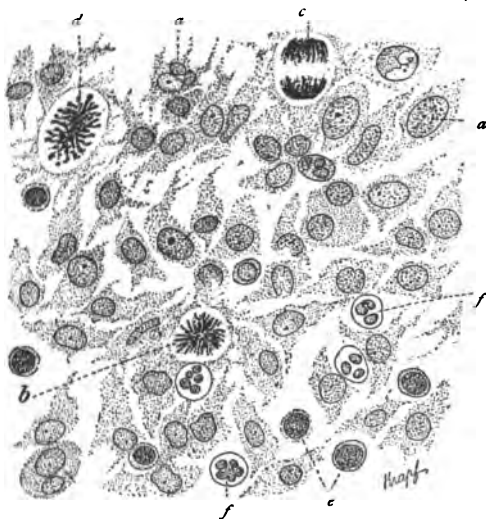
3. Intense Vascular Reaction. Suppurative Inflammation.
—When pyogenic microorganisms are carried into a wound and conditions are favorable for their growth, a more intense grade of inflammation is excited, which is usually of the type called "suppurative." This process is best followed in tissues into which pure cultures of pyogenic cocci have been injected experimentally.

Within four hours after such injection the vessels in the neighborhood have been found to be gorged with blood, the

blood current slowed, and leucocytes increased in number and partly adherent to the vessel walls. Such a condition is termed acute congestion.

After ten to twelve hours increasing numbers of leucocytes have emigrated from the vessels until the tissue is thickly infiltrated by these wandering cells lying in the distended lymph spaces. Diapedesis of red cells occurs in greater or less degree, and exudation of fluids from the blood is, in some cases, a prominent feature.

FIG. 11.



GRANULATION TISSUE. (Coplin.)

a, round cells before mitosis; *b*, monaster; *c*, diaster; *d*, formation of the skein; *e*, lymphocytes; *f*, polynuclear leucocytes.

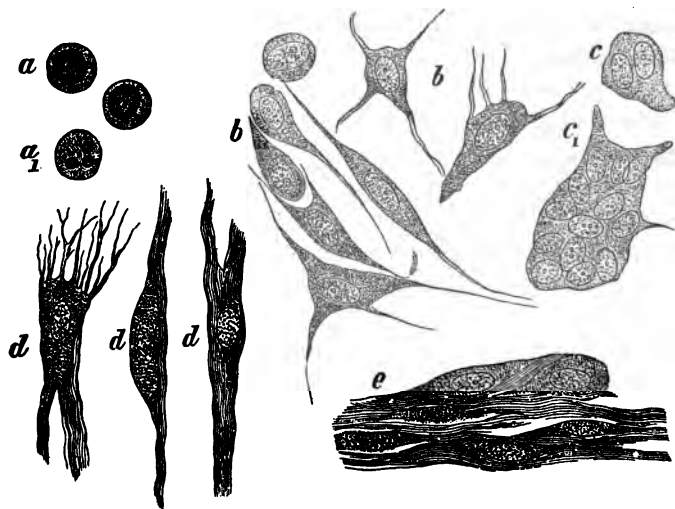
When such an inflammation occurs in a superficial surface, such as a mucous membrane, the emigrated leucocytes, extruded red cells, exuded serum and exfoliated lining cells form a copious purulent discharge from the surface, and do not damage the tissue by being retained under pressure. In deeper tissues, from which the exuded elements do not readily escape, their presence

is more serious, and tends to obstruct the flow of blood and to lead to degenerative changes in the tissue cells of the affected region. Nevertheless, in either situation the process may not go beyond the infiltration of the tissues with leucocytes and serum, and resolution follows without permanent damage to the tissue. (*Lobar pneumonia.*)

Healing of simple suppurative inflammations takes place after the subsidence of vascular disturbance, by the absorption of fluid exudate, and the liquefaction (largely by digestive ferments), and absorption of the cellular exudate.

Healing by Granulation Tissue.—When suppuration occurs in surgical wounds all attempt at cohesion of surfaces commonly

FIG. 12.



CELLS FROM GRANULATION TISSUE. (Ziegler.)

a, a₁, mono- and polynuclear leucocytes; *b*, forms of mononuclear new cells; *c, c₁*, bi- and polynuclear new cells; *d, e*, two stages of development of connective tissue from the new cells.

fails and the wound is closed from the bottom up by a slow process called healing by granulation. Here, after partial sub-

sidence of exudation, new capillaries, forming minute projecting tufts, supported by new connective-tissue cells, with a little intracellular substance and many wandering cells, develop from the cut surface, forming what is known as granulation tissue. Such tissue has a granular surface, owing to the projecting tufts of vessels. By gradual increase in the quantity and density of the intracellular substance, disappearance of cells and obliteration of vessels, the tissue is transformed into dense connective tissue forming a scar or cicatrix. Epithelium finally covers over the wound by gradual proliferation inward from the cut edges.

Inflammatory Reaction with Local Death of Tissue. Necrotic Inflammation.—When bacterial inflammation reaches a suppurative grade in a confined tissue it seldom resolves without causing some death of tissue and forming an abscess. The additional element of death of tissue throws this process into the class of necrotic inflammation.

The course of events in abscess formation has been very carefully followed experimentally. The affected tissue becomes so thickly infiltrated with leucocytes and so much distended by exuded fluids that the vessels are compressed and occluded. All tissue cells thus cut off from nourishment promptly undergo acute necrosis and become more or less fluid. In some cases death and liquefaction of tissue occur apparently before there is sufficient exudate to compress the vessels, and the death of tissue is then referable principally to the necrotic action of bacterial toxins.

Sections through the region of an abscess disclose the presence of (1) a central cavity containing semi-fluid necrotic material composed of fragmented tissue cells, leucocytes, red cells, and usually an abundance of microorganisms. About this area there is (2) a zone of tissue in a state of intense purulent infiltration, while still further from the necrotic center (3) the tissues are in a state of intense congestion. Microorganisms in variable numbers may be found, partly in tissue spaces, partly englobed

in tissue cells and leucocytes, in all parts of the abscess-wall, even to the edges of the congested area.

Healing of an abscess progresses slowly and is greatly facilitated by evacuation of the contents of the cavity and approximation of its walls. The vascular disturbance may then rapidly subside, exudation decreases, proliferation of connective-tissue cells and blood-vessels begins, and healing progresses as after simple suppurative inflammation, with the development of granulation tissue. A form of secondary cohesion of the abscess walls may occur which greatly diminishes the space to be filled by granulation tissue. All dead tissue is replaced, not in its original type, but invariably by granulation tissue and its final product, cicatricial tissue.

When the abscess is not evacuated healing is much slower. While considerable amounts of necrotic material may be removed by absorption and its remaining bulk largely reduced by desiccation, large abscesses often leave some necrotic matter which becomes surrounded by a fibrous wall and encysted. When the abscess is evacuated, but the walls are held apart, suppuration continues, the walls become lined by granulation tissue, which, being highly inflamed and discharging considerable pus, is sometimes called a pyogenic membrane. (*Chronic empyema.*)

Inflammatory Reaction with Diffuse Death of Tissue.

Diphtheritic Inflammation.—Some intense chemical irritants and some bacteria, notably the bacillus of diphtheria, when acting upon mucous membranes, excite an intense grade of inflammation characterized by considerable fibrinous and purulent exudation, and rapid death of superficial tissues. The coagulated fibrin entangling the elements of necrotic tissue tends to form a false membrane adherent to the surface of the inflamed part, whence the term pseudo-membranous inflammation is often applied to the process. Some forms of spreading suppurative inflammation of deeper parts cause rapid death of

considerable areas of tissue, and much fibrinous exudate, and some writers apply the term diphtheritic inflammation to this process also. (*Diphtheritic erysipelas*.) Healing, if it occurs, follows the same course as in simple necrotic inflammation.

Gangrenous Inflammation.—In some forms of virulent and specific bacterial infection, but also as a result of cold, heat, pressure (bed-sores), ergot poisoning, and disease of the nervous system (syringomyelia), necrosis of tissue occurs rapidly and affects considerable areas. This type of inflammation is called gangrenous and the process gangrene. The necrosis is here the result of the necrotic action of bacterial toxins or of compression of blood-vessels with anemia, or of the peculiar effects of heat, cold, etc. The dead tissues remain for a time attached to the living, but may be eventually thrown off as a slough or sphacelus by the exudation of leucocytes and serum at a line of demarcation. When the tissues remain moist from the presence of much inflammatory exudate the term moist gangrene is applied. Often there is little exudation, and the evaporation of fluids leaves the dead part comparatively dry (dry gangrene, mummification). Most bacterial infections induce moist gangrene. Senile gangrene, due to disease and occlusion of peripheral arteries, and most other non-bacterial varieties tend toward desiccation and dry gangrene. Some specific bacteria which often excite gangrenous inflammation are active gas-formers, and the resulting sphacelus contains many gas-bubbles and is emphysematous (*Bac. aerogenes capsulatus*, *putrefactive species*).

When simple suppurative inflammation attacks the periosteum of long bones, conditions are peculiarly favorable for the occlusion of the nutrient artery supplying considerable areas of the shaft of the bone. When these vessels become occluded considerable areas of the shaft become necrotic and the dead mass is slowly extruded by reactive inflammation as a sequestrum.

Invasion of the Blood Stream by Bacteria.

Septicemia, Bacteremia.—In all the bacterial inflammations thus far considered, the bacteria are confined more or less completely to the site of the local inflammation and none or very few reach the general circulation. In some very virulent infections in susceptible individuals, bacteria reach the general circulation and are to be found nearly constantly in cultures of the blood. This condition is called septicemia.

There is considerable latitude in the present application of the term septicemia. Some apply it indiscriminately to any condition in which there are symptoms of grave constitutional disturbance from absorption of toxins from a local inflammatory focus even when no bacteria can be found in the blood. This usage robs the term of special significance, since there is more or less absorption of toxins in all inflammatory processes. It is better to limit the term to those conditions in which bacteria may be found in the blood, the best example of which is found in the idiopathic form of general infection of the blood by the *streptococcus pyogenes*. It remains true, however, that bacteria may be discharged into the blood from inflammatory foci at intervals, but if promptly removed by leucocytes and endothelial cells they cannot be demonstrated in the blood by cultures.

If the trend of usage should limit the term septicemia, as present indications seem to contraindicate, to that somewhat characteristic set of clinical symptoms which is associated with profound intoxication by bacterial products, then the invasion of the blood stream by the bacteria themselves may be designated as bacteremia. At present clinicians use the term septicemia rather constantly to imply that there is invasion of the blood stream by bacteria, and the latter unequivocal term is, for this and other reasons, comparatively unrecognized.

In some cases of bacterial invasion of the blood the micro-organisms are carried by the blood current to distant organs in which they lodge and give rise to local metastatic abscesses.

Such a condition is termed pyemia. In cases of pyemia, cultures of the blood are usually negative till shortly before death.

In some cases there are symptoms of profound intoxication by bacteria and their products, as well as the development of metastatic abscesses and the condition is sometimes termed septicopyemia.

Resumé.—It thus appears that the inflammatory process may consist in :

1. A reaction limited entirely to the fixed cells of the tissue, or
2. A cellular reaction plus congestion of the vessels, or
3. Cellular reaction with congestion, to which is added exudation of blood cells and serum, or
4. Cellular reaction may be delayed and the exudation may be very prominent and consist largely of leucocytes (suppurative inflammation), or
5. To the suppurative process may be added death of tissue and abscess formation (necrotic inflammation), or
6. Necrosis of tissue may be prominent from the first (diphtheritic inflammation), or
7. Rapid necrosis of large areas of tissue may be the chief feature (gangrenous inflammation), or
8. Bacteria may temporarily or permanently invade the blood stream (septicemia, bacteremia).

THE SEPARATE FACTORS IN EXUDATIVE INFLAMMATION.

We have thus far indicated the phenomena which occur in the different grades of acute inflammation. It is necessary to consider more in detail some of the processes concerned.

The Vascular Changes.

After the initial acceleration of the blood current the slowing of the local circulation may progress until there is little or no movement of the blood, and a condition of partial or complete

stasis is established. This is often followed by coagulation of the blood in the vessel, which thus becomes thrombosed. If the thrombosis occurs in large or medium-sized vessels a portion of the thrombus may be dislodged and, reaching the blood current, may be carried to distant organs till it lodges in a smaller vessel. This process is called embolism, and the lodging mass an embolus. Emboli containing bacteria are probably the means of origin of many metastatic abscesses in pyemia.

Infarction.—Areas of tissue cut off from their blood supply by embolism undergo a series of changes, tending toward necrosis. This process is called infarction and the affected area an infarct. When blood from collateral vessels makes its way from behind into the infarcted area, this area becomes engorged with blood by the backward flow, and the natural forces of circulation being cut off, the blood coagulates in the infarct. This process is called red infarction. In certain tissues collateral circulation is very imperfect (brain), no backward flow is established, the infarcted area remains bloodless and light-colored, and the process is called white infarction.

The Fluid Exudate.

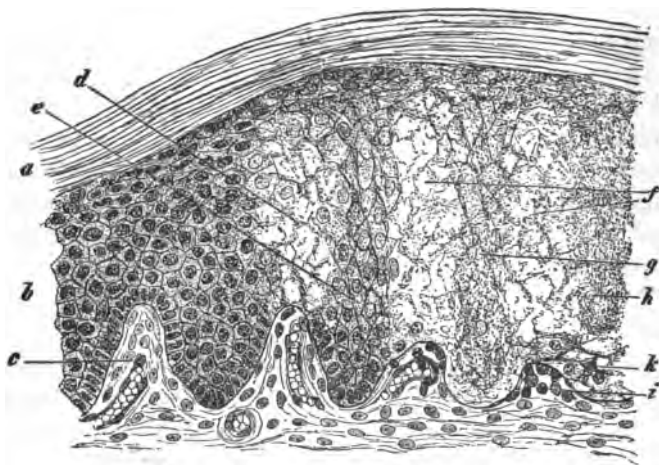
Another important series of vascular changes is largely dependent upon stasis in vessels in inflamed tissues. (1) Owing principally to lack of nutrition, the endothelial cells become swollen and the spaces between them become wider, which favors not only the exit of blood cells but also the passage of blood-serum. Other factors favoring the exudation of serum are: (2) the increased blood-pressure in the distended vessels, (3) alteration in the composition of the blood, (4) changes in osmotic tension of the intracellular fluids, while it is probable (5) that the irritated endothelium exerts a secretory action in the exudative process. Owing to different combinations of these factors the quality of the exudate varies widely.

When increased blood-pressure alone is present, as in cases of chronic endocarditis, the discharged fluid is called a transudate

and contains only a small proportion of the more easily diffusible albumin of the blood, serum-albumin.

When a true inflammatory process affects a connective-tissue or serous membrane, the exudate usually shows a higher proportion of albumins and a larger ratio of the less diffusible blood-albumin, serum-globulin, of which the presence indicates a more serious alteration in the vessel wall. Tissues infiltrated by these fluid exudates are said to be edematous, are in a state of edema.

FIG. 13.



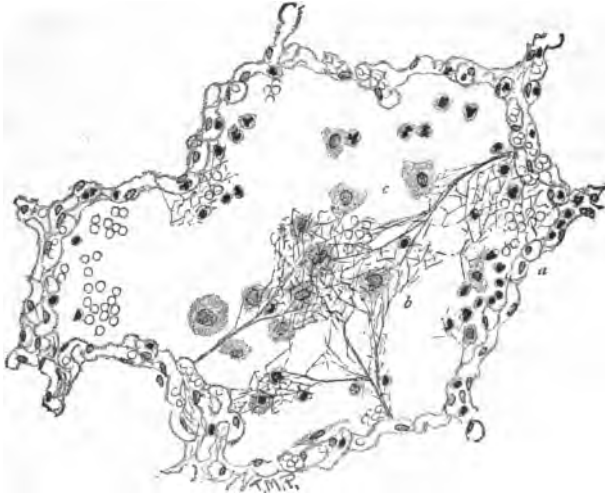
SECTION OF A VESICLE FROM BURN. (Ziegler.)

a, horny layer; *b*, rete Malpighi; *c*, normal papilla; *d*, hydropic cells of the rete, the nuclei still visible in places; *e*, interpapillary epithelia; below normal, above drawn out and swollen; *f*, cells entirely fluid; *g*, interpapillary epithelia, swollen, nuclei lost, loosened from the cutis; *h*, more complete destruction of cells; *i*, papilla, depressed and infiltrated with round cells; *k*, fibrin.

(*Passive and inflammatory edema.*) Some forms of inflammation are characterized by the exudate of much fibrinogen, which soon coagulates, yielding a fibrinous deposit. (*Illus. Lobar pneumonia, Fibrinous pleurisy.*) In suppurative inflammation the exudate is composed of variable quantities of serum-albumin,

globulin, fibrin and leucocytes. While albumin, globulin, and, in most cases, fibrin, are usually completely absorbed in the healing process, the presence of many leucocytes in the interstices of a tissue is commonly followed by a more or less permanent deposit of mucin, and recovery of function is slow or incomplete. It is for this reason that a purulent infiltration has a more serious prognosis than a simple serous process. (*Empyema in children and adults.*)

FIG. 14.

EXUDATIVE INFLAMMATION IN THE LUNG. (*Delafeld & Prudden.*)

a, alveolar wall; *b*, fibrin, entangling *c*, epithelia.

The Cellular Exudate.

(*a*) **Red Cells.**—The diapedesis of red blood cells is a very prominent feature of some exudative inflammations. Their exit results from a loss of continuity of the vessel wall and from increased blood-pressure. Such exudates are blood-stained or bloody, and are described as sanguinolent or sero-sanguinolent according to the proportion of serum in the exudates. Bloody

exudates usually indicate an intense form of bacterial infection, and the loss of blood is most abundant in the early stages of the process. (*Pneumonia in infants.*) Very vascular tissues most often yield hemorrhagic exudates and some pathogenic bacteria have a special tendency to excite hemorrhage. (*Bac. coli communis*, *Bac. tuberculosis.*)

Hemorrhagic diathesis is a term applied to an obscure constitutional predisposition toward hemorrhages, which here occur from slight traumatism or ordinary bacterial inflammations.

(*b*) **The Leucocytes in Inflammation. Leucocytosis.** The importance of leucocytes in inflammation has been clearly shown in the lower metazoa, in their behavior toward foreign bodies, which they englobe and digest or excrete. Although several varieties of new cells are found in inflamed tissues, the polynuclear neutrophile leucocytes are the most important variety, and it is an increase of this variety of cell which is usually indicated by the term leucocytosis.

In nearly all forms of exudative inflammation, especially in the suppurative type of bacterial origin, the leucocytes have an extremely important part to fulfill. In the early stages of the process the congested vessels are usually found to contain an excess of white cells, which it can be positively stated are attracted to the locality by the presence of bacteria and their products. This attractive force has been called, as stated, positive chemotaxis. Negative chemotaxis or a repelling force of bacteria upon leucocytes probably exists, but it is extremely difficult to find any clear illustration of it. So active is this attractive force that the leucocytes will sometimes overcome considerable obstacles in order to reach the bacteria.

It might be supposed that the mechanical sifting of the cohesive leucocytes by the swollen endothelium may explain much of the local afflux of leucocytes, but it has been shown that the attractive force is exerted not merely in the inflamed focus but at a distance. Moreover, all the local changes in the blood-ves-

sels may exist in some forms of inflammation without any local afflux of leucocytes. (*Diphtheria in susceptible animals.*) Further, in most bacterial infections the leucocytes are increased in number not only around the inflamed tissue but throughout the general circulation as well, and in their sites of origin, the lymphoid tissues, pronounced evidence of increased formation of leucocytes has been found to accompany distant suppurative inflammations. We have, therefore, to distinguish—(1) a local and (2) a general in travascular increase of leucocytes, or leucocytosis.

Significance of Leucocytosis.—A long series of experiments has shown that the leucocytes are one of the important means of defense of the animal organism against bacterial invasion. (See Immunity, Pt. II.)

If sections are made of tissues one hour after the subcutaneous injection in a rabbit of *bac. pyocyaneus*, the area surrounding the bacteria is found to be anemic, while the leucocytes are present in scanty numbers, having been apparently repelled or at least not attracted by the bacteria. This period corresponds to a stage of negative chemotaxis which occurs at the beginning of most infectious disease and lasts a variable time, continuing until death in some virulent infections in susceptible animals and persisting only a few minutes or hours in milder infections or in refractory subjects.

If the sections are made several hours after the injection, the leucocytes are found to have gathered in large numbers at the site of the inoculation. Many white cells are found to have been destroyed by the bacteria and their products, but others are seen to have englobed the bacilli which may be found in various stages of degeneration. Under favorable circumstances the leucocytes succeed in englobing and destroying all the bacteria, after which healing occurs as with aseptic wounds. The power to englobe and destroy bacteria is called phagocytosis.

There are great variations in the phagocytic power exhibited by leucocytes of different animals toward pathogenic bacteria,

and this power is capable of being greatly increased by artificial immunization of the animal.

It appears to be a general rule that bacterial infections which pursue a favorable course are attended by marked local afflux of leucocytes which limit the growth of the microorganisms, while in unfavorable cases there is little or no leucocytosis, and the bacteria spread rapidly through the tissues causing the death of the animal. A practical illustration of this rule is seen in the well-known favorable significance of laudable pus, of which the yellowish color indicates a large proportion of leucocytes. In spreading necrotic inflammations, on the other hand, a thin sanious pus is commonly discharged which contains comparatively few leucocytes. Exceptions to the above rule are found in the *bacillus of tuberculosis* and less completely in the *bacillus typhosus*, which have little or no tendency to attract leucocytes or at least affect only one of the less numerous of the varieties of white blood-cells, the mononuclear.

Further support of the importance of phagocytic properties of leucocytes in inflammation is found in the marked bactericidal action of purulent fluids in the test-tube. While many body-fluids, including blood-serum, exhibit considerable power in inhibiting the growth of bacteria in the test-tube, the most actively bactericidal animal fluid yet discovered was obtained from a purulent exudate into the pleural cavity excited by an aseptic irritant.

Before leaving the subject of phagocytosis it is necessary to emphasize the fact that the leucocytes are not the only elements in the body which exert bactericidal and phagocytic properties in inflammation. The blood-serum, as has been said, lymph, and mucus, exhibit varying degrees of bactericidal activity while endothelial, epithelial, visceral, and connective-tissue cells all exhibit more or less phagocytic power. (Phenomenon of Pfeiffer.) Although there has been much conflicting evidence, it may safely be said that the leucocytes are important agents in limiting bacterial infections, while essential aid in the function

is furnished by tissue cells and by tissue fluids. Local leucocytosis, therefore, indicates the effort to limit the spread of bacterial infection, while the intravascular leucocytosis measures the same effort to furnish leucocytes at the site of infection, and to rid the blood and system of absorbed bacterial products.

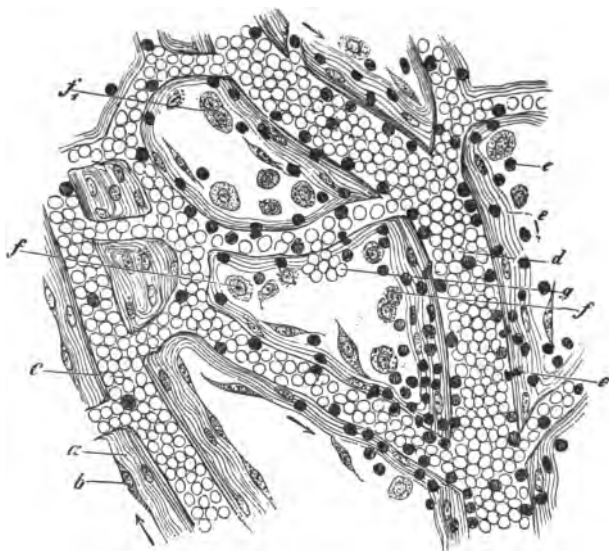
Eosinophile Cells in Inflammation.—Some forms of exudative inflammation are attended by a local increase in the number of eosinophile leucocytes. These cells are very actively ameboid and emigrate from the vessels as do the neutrophile leucocytes. Eosinophile leucocytes are susceptible to chemotactic influences, as are neutrophile, but the chemical substances exerting the influence are peculiar. Ordinary excitants or inflammation have no attraction for eosinophile cells, but in many subacute or chronic inflammations, especially in the skin (*pemphigus*) or mucous membranes (*chronic bronchitis*) there may be a rich local eosinophile leucocytosis. A marked increase of these cells in the general circulation may accompany this local afflux, as these cells are derived from the bone-marrow, although multiplying to some extent after lodgment in the inflamed focus.

Lymphocytes.—In some forms of inflammation, especially of the subacute or chronic type, many lymphocytes gather at the inflammatory focus. As these cells are not lacking in ameboid property they may respond to chemotactic influences, and their local afflux may also be assisted by purely mechanical causes. It is a rule that those inflammations which exhibit a special tendency to affect the lymphatic system and to spread through lymph-vessels induce lesions in which many lymphocytes are found. (*Tuberculosis, Peri-arthritis.*)

Plasma Cells.—In subacute and chronic inflammations some of the new mononuclear cells are larger than the lymphocytes, possess a well-defined layer of homogeneous basophile protoplasm, and a single compact and usually eccentric nucleus. These cells have been termed plasma cells, and much has been written on their relation to forming connective tissue. Their

origin and significance is uncertain, but they are distinguishable from large lymphocytes by special stains.

FIG. 15.



INFLAMED MESENTERY. (*Ziegler*.)

a, connective tissue, covered by *b*, normal epithelium; *c*, small artery; *d*, vein, leucocytes clinging to wall; *e*, leucocytes in emigration; *f, f1*, desquamated epithelia; *g*, red cells after diapedesis.

The Changes in Fixed Tissue Cells in Exudative Inflammation.

As already stated, the initial injury which leads to inflammation always first affects the cells of a tissue, causing some degree of degeneration. Some cells coming into immediate contact with the injurious agent are at once rendered necrotic, and the earlier stages of degeneration are better studied in regions subjected to less violent action. The cells of the renal tubules furnish illustrations of well-defined stages of cellular degeneration. An earlier stage of degeneration is seen in the chromatolysis which ganglion cells suffer under some injurious influences.

Regenerative Changes in Cells in Inflammation.

We have thus far considered only the degenerative inflammatory changes in cells, but inflammation commonly induces some very important regenerative processes in the affected cells. Very remarkable examples of reproductive activity of injured cells are seen in some very low animals (thus hydra develops an entire set of tentacles about points of incision on its stem). Among vertebrates whose tissues are more highly differentiated acute inflammation causes more degeneration than regeneration, especially in the areas most intensely inflamed, but in surrounding areas marked evidence of proliferation of cells is usually observed, and it has already been mentioned that the healing process is largely the result of the regenerative activity of endothelial and connective-tissue cells.

In fibrino-purulent inflammations of serous membranes very striking illustrations are seen of the proliferating tendency of inflamed endothelium.

Subacute inflammation of serous membranes may consist almost entirely of congestion of vessels and proliferation of large numbers of lining cells and fibroblasts, but with little or no exudation. This process is therefore sometimes called cellular inflammation. The product of such an inflammation is at first a tissue composed largely of the new cells with a little intracellular substance and some new blood-vessels. Later the tissue shows many of the characters of fibrous connective tissue.

Very pure examples of the inflammatory growth of new connective tissue are seen in some subacute inflammations of the kidney, where the chief alteration observed is an increase in the quantity of the supporting stroma of the organ. This new tissue is composed of new branching fibroblasts (connective-tissue cells) and considerable moist finely fibrillated intracellular substance.

In tuberculous and syphilitic inflammations the chief result may be a proliferation of fibroblasts and endothelial cells but

usually there is a moderate exudation of leucocytes and serum, producing a peculiar type of tissue called tubercle tissue, consisting of granular intracellular substance, large epithelioid fibroblasts, mononuclear and polynuclear leucocytes, and giant cells. The giant cells are a very characteristic feature of tubercle tissue, being formed usually by the fusion of several cell-bodies with multiplication of nuclei. They are occasionally seen in exudative inflammation from other causes. In some tuberculous or syphilitic foci, there gather large numbers of mononuclear leucocytes or lymphocytes, which form a characteristic type of tuberculous nodule, called the lymphoid tubercle.

Those forms of inflammation which consist largely in the production of new tissue are called productive inflammations. The two main types of inflammatory reaction may now be said to be (1) the exudative and (2) the productive. A great many examples exist of mixed exudative and productive processes. While the final product of productive inflammation is nearly always fibrous tissue, it by no means follows that all this fibrous tissue is to be classed as true connective tissue. True connective tissue probably arises only from preëxisting connective-tissue cells, while the fibrous areas which result from proliferating endothelium, epithelium, and leucocytes, have a somewhat different significance. Nevertheless, it is practically impossible to determine the true origin of all the fibrous products of chronic inflammation, and equally difficult to follow the fate of many exuded leucocytes which are nearly constantly found in inflammatory new connective tissue. The burden of proof lies with those who claim that leucocytes may be transformed into fibroblasts, which has not yet been demonstrated. Endothelium may undoubtedly produce a tissue which closely resembles connective tissue, but of leucocytes it can only be said that most of them disappear or retain the character of wandering cells, and that mononuclear leucocytes sometimes become passively incorporated in new connective tissue, without contributing essentially to its formation.

Inflammatory and Non-Inflammatory Fibrous Hyperplasia.

While many deposits of new fibrous tissue can with certainty be referred to an inflammatory process, fibrous overgrowth often occurs under conditions which render an inflammatory origin very improbable. Thus, the dense connective tissue found in old cases of nephritis or cirrhosis of the liver is clearly the result of a previous productive inflammation. Similarly the areas of connective tissue which replace an infarct of the spleen are plainly referable to a reactive inflammation excited by the necrotic tissue of the infarct.

On the other hand, the extensive overgrowth which occurs in the female breast after the menopause is certainly not referable to inflammation, nor is it of neoplastic origin. The fibrosis which occurs in the lateral tracts of the spinal cord in cases of cerebral apoplexy has none of the distinct antecedents of inflammation but merely follows the atrophy of the medullated fibers whose cells of origin have been destroyed by a cerebral hemorrhage.

It is therefore necessary to distinguish between inflammatory and non-inflammatory fibrous hyperplasia. The majority of non-inflammatory hyperplasias are believed by many to be referable to disordered nutrition of the part, the relatively low type of fibrous tissue persisting and even increasing in nutritive conditions which are unsuited to cells of higher function. Thus replacement fibrosis occurs in the heart in proportion to atrophy of the muscle cells and the simplest form of this is seen as a senile change; it is called fibrous myocarditis, but is not strictly an inflammation or the result of it and hence does not deserve the termination -itis. Similar fibrosis may occur in nearly all tissues.

Marked grades of inflammatory hyperplasia are seen in other tissues. The lymph-nodes in the neighborhood of an infected wound are often found much enlarged, partly from hyperemia, or exudation, but principally from a marked increase in the num-

ber of lymphoid cells, which are actively stimulated to new production by the irritant.

Subacute and chronic inflammations of mucous membranes, especially of the nasal and uterine mucosæ, often result in much increase both of the cells and fibers of the stroma and in the number, length and tortuosity of the glands. Some of the inflammatory hyperplasias in mucous membranes reach almost to the grade of neoplastic growth.

Cell Division.—Part of the process of repair consists in cell reproduction. This occurs when an injured tissue is regenerated or its place taken by other tissue cells, regeneration being less common in higher animals than repair. Cells multiply in two ways, indirectly, by karyokinesis, karyomitosis or simply mitosis, and directly by amitosis; the former is by far the more frequent.

A cell is a microscopic mass of protoplasm provided with a nucleus and exhibiting function, and is the ultimate physical unit of plants and animals. Roughly the cell may be divided into cell body or protoplasm, nucleus, enveloping membranes and certain other structures, as appears from the diagram :

FIG. 16.

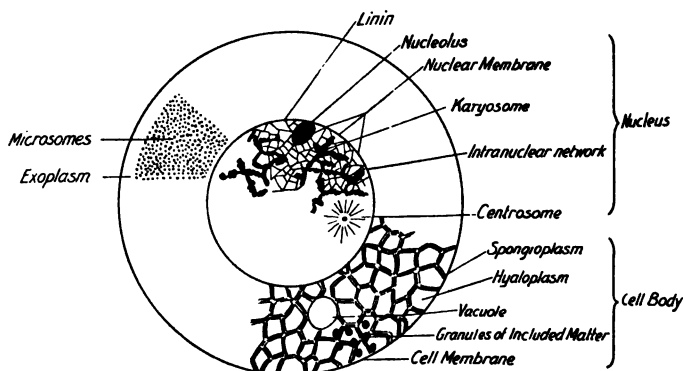
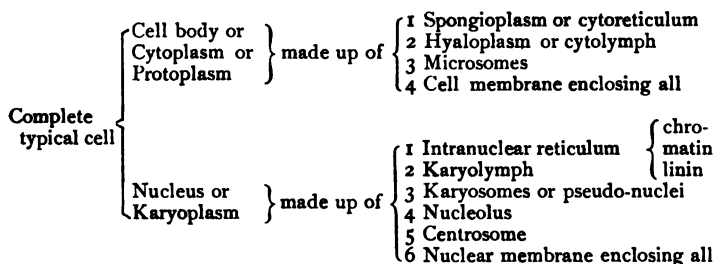


DIAGRAM OF THE PARTS OF A CELL. (A. E. T.)

SUMMARY OF THE PARTS OF A COMPLETE TYPICAL ANIMAL CELL.



The cytoplasm is granular or homogeneous and consists of a meshwork of spongioplasm, called the cytotreticulum, enclosing in its spaces the fluid hyaloplasm, the proportion between these two elements varying from time to time and in different cells, as a rule the younger cells having relatively more hyaloplasm and less spongioplasm and the older the converse of this. Imbedded in the cytoplasm are many fine granules called microsomes, which are seldom uniformly distributed, being less numerous about the periphery (exoplasm) and often gathered in certain sections of the cytoplasm; if very numerous these microsomes give the cell body a dark look. Fragments of foreign matter and empty spaces or vacuoles are also common appearances in the cell body.

The nucleus is the focus and source of the cell's activity; usually it lies well within the cell body but occasionally it stands out like the cornea on the sclerotic. It bears a certain relation to the size of the cell but may occupy nearly the whole of the cell membrane's capacity (lymphocyte). In form it is spherical, ovoid or irregular, and may be single or many. The only cells normally without nuclei in the human body are those of the epidermis (outer layer), of the terminal respiratory passages and the red blood cells. The resting nucleus shows a nuclear membrane of two layers, the inner staining and called the chromatic, the outer taking no stains and called the achromatic layer. This encloses the karyoplasm which is made up of a double network

and lymph in the meshes, called karyolymph. The network shows delicate fibers which do not take stains, called linin, and which support the heavier and nodular reticulum of chromatin, which is the element with special affinity for nuclear stains ; in the latter certain nodal points of thickened material are called karyosomes and simulate nuclei ; the chromatin may be threads, rods or granules. The nucleolus, or true plasmasome, is a small body of unknown function which takes the nuclear stains with avidity, lying free in the cavity of the nuclear membrane or attached by linin fibers ; at the beginning of division it is extruded and disappears, to return at a later stage.

The centrosome is a small spherical body which acts as the directing force in the arrangement of the chromatin bundles during division ; it is then surrounded by a halo of rays which together make the attraction sphere or archosome.

The nuclear and cell membranes are comparatively unimportant envelops for the elements of each.

Function. Broadly grouped all the activities of cells fall under one of the following heads :

1. Movement, which may be protoplasmic, ameboid, or ciliary ; that is, there may be currents of flow in the cytoplasm, or the cell may put out large processes, pseudopods, or it may be provided with fine projecting hair-like processes which keep up a lashing motion.
2. Irritability, by which is meant the response to external stimulus, mechanical, thermic, photic, electric, chemic, positive or negative cyto-taxis.
3. Metabolism, consisting as elsewhere of anabolism or true nutrition and catabolism or waste and excretion.
4. Reproduction, by mitosis, that is indirectly, or by amitosis, directly.

Cell kinesis. In the indirect form of reproduction the various parts of the cell exhibit a number of complicated movements and

divisions, the energy therefor being doubtless derived from chemical energy set free in the course of the cell's metabolism and stored toward the end of the resting stage. It is usual to describe the process in four stages, each called a phase, the entire series taking from 30 minutes, in man, to five hours, in amphibia :

- I. Prophase. The nucleus prepares for the coming division, it enlarges ; the centrosome passes out into the cytoplasm and divides, the first actual division in the process, rarely it divides before extrusion ; the daughter centrosomes moving then to opposite poles of the nucleus, each surrounded by its rayed attraction sphere or archo-

FIG. 17.
Polar radiation. Nuclear spindle.



SCHEME OF THE MOTHER STAR. (*Stokcr.*)

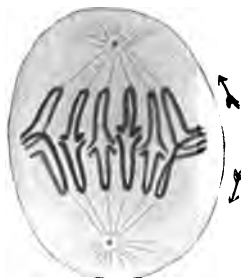
Two centrosomes, equatorial plates of divided V's, spindle and attraction spheres, the whole surrounded by cytoplasm at the beginning of the metaphase.

some ; the rays passing from one centrosome to the other arranged as a spindle of threads (linin) in equidistant meridians ; along these the chromatin rods are directed. The entire figure of centrosomes, rays about each, and certain rays common to both making the spindle, closely resembles the lines of magnetic force

along which particles of iron arrange themselves on a paper when the two poles of a magnet approach it from below. The chromatin threads become less numerous, shorter and thicker, arranged in a tangle or wreath. The nucleolus and nuclear membrane disappear. The chromatin is now arranged in short rods, each bent in the middle to less than a right angle, forming a V; varying in different animals from 2 to 36, for man 16; the V's collect at the equatorial plane of the spindle, the angles turned in to the main axis of the spindle, thus making the equatorial plate or monaster.

2. Metaphase. The V's split along their length so that a double equatorial plate is formed and each group of halves begins to draw toward its cor-

FIG. 18.

SCHEME OF METAPHASE. (*Stohr.*)

Two centrosomes, spindle, and dividing chromatin V's, surrounded by cytoplasm.

responding pole or centrosome, angle first. This is the second actual division of cell elements.

3. Anaphase. The divided V's are collected about each centrosome, forming the diaster, and an indentation appears in the cytoplasm at the level of the equatorial plane. This is the third division.

4. Telophase. This constriction moves inward along the mid-transverse plane and completes the di-

FIG. 19.

SCHEME OF THE EARLY ANAPHASE. (*Stohr.*)

Divisions of chromatin complete, the half V's collected at each pole.

vision of the cell ; each half containing exactly half of the chromatin half-V's, one of the daughter centrosomes and half the cytoplasm. In each part a nucleolus and a nuclear membrane appear and the resting stage is again attained. The essential element in this process is

FIG. 20.

SCHEME OF THE EARLY TELOPHASE. (*Stohr.*)

Cytoplasm incompletely divided, centrosome in each nucleus, chromatin still disposed in V-shaped figures as it arrived in each, but beginning to branch into network, nuclear membrane forming.

the chromatin, and hence its rods and V's are regarded as the carriers of hereditary characters.

In amitosis, which in the human being is seen only in leucocytes, lymphocytes and the cells of some neoplasms, the nucleus simply constricts, its halves draw apart, and with this a constriction appears in the cytoplasm; both nucleus and cytoplasm occasionally lengthen out to fine threads before completely dividing.

Abnormal examples of mitosis are found in which there are more than two centrosomes (called multipolar), or where the equatorial plate divides into more than one set of split V's, or the diaster may divide secondarily; and in others, perhaps under conditions of pressure and rapid division, the nuclei divide and redivide while the cell body remains undivided, only enlarging to accommodate the numerous nuclei, and thus forming giant cells. Experimentally some of these abnormal forms may be reproduced by treating the dividing cells with various chemical solutions which irritate or inhibit in some unexplained way, or by mechanically unfavorable conditions.

A form of abnormal direct division is known as nuclear fragmentation or karyorhexis.

Young cells produced as above resemble the parent cell; a connective tissue or a cartilage cell would not divide into two epithelial cells. The life of all cells is limited and as they grow old there is a decrease in the volume of both nucleus and cell body with irregularities in the chromatin; vacuoles may appear even in the nucleus. The growth of cells is rarely symmetrical; usually it follows two axes, a major and a minor, making elongated, cylindrical and flattened figures; pressure from surrounding cells doubtless is of great influence here, both direct and transmitted.

Cells are held together by products of their own metabolism (cement substance) which is often homogeneous but may take on a fibrillar structure; other products are held in the cell or removed for elimination.

INFLUENCE OF THE NERVOUS SYSTEM UPON INFLAMMATION.

The nervous system has a prominent influence in controlling the vascular phenomena of inflammation, for if its influence is cut off the stage of exudative inflammation follows more rapidly than in a normally innervated part. (*Inflam. of rabbit's ear after section of nerves.*)

If the sympathetic nerve filaments passing to the rabbit's ear be divided, the vessels dilate, inflammatory changes when excited follow rapidly and healing is likewise more prompt. If, however, the spinal cord filaments be divided, the vessels contract under the influence of the sympathetic, and inflammatory changes follow traumatism more slowly, exudative phenomena are less marked, but stasis is more apt to occur in the vessels and gangrene more frequently follows upon injury. These interesting experiments illustrate the difference in the action of the two sets of nerves, but do not appear to have a wide practical application. The peripheral network of nerve filaments and ganglion cells immediately surrounding arterioles and capillaries appears to be purely sensory, and the effects of the inflammatory process resulting from its destruction have not been determined.

It is an important fact that inflammation in an area supplied by one portion of a nerve trunk may excite some inflammatory disturbance in areas supplied by other portions of the same trunk. (*Redness of the face with toothache. Sympathetic ophthalmia.*)

Finally, cerebral nervous influences have undoubtedly alone induced inflammatory phenomena. (*Hypnotic suggestion of red-hot poker.*)

CLASSIFICATION AND NOMENCLATURE OF INFLAMMATIONS.

Inflammations are classified according to the most marked feature of the inflammatory process, which varies with the struc-

ture and position of the tissue affected and with the nature and intensity of the irritant.

The termination *-itis* has been tacitly agreed upon to represent inflammation of the part whose name precedes it, as bronchitis, peritonitis. This termination is derived from the Greek adjective ending in *-ιτης* and some word for disease (*νόσος*) is understood. Certain inflammations do not carry this ending, as pneumonia for inflammation of the lungs, angina for inflammation in the tonsils and floor of the mouth, and phlegmon for subcutaneous inflammation. The prefix *peri-* indicates that the inflammation is in the immediate neighborhood of an organ, sometimes in its capsule, as periarteritis, perisplenitis, or is in a serous membrane, as pericarditis; the prefix *endo-* refers to inflammation of the lining of hollow organs, as endocarditis; *para-* locates the lesion in adjacent connective tissue, as parametritis. This usage is not always consistent.

1. Degeneration.

The inflammatory process may not go beyond degeneration, followed by regeneration of tissue cells, while vascular phenomena are almost entirely wanting.

Very mild chemical irritants or traumatism applied to cutaneous or mucous surfaces or affecting deeper tissues may cause only a certain grade of degeneration of tissue cells, which is promptly repaired without vascular disturbance. In the infectious diseases all the internal viscera are exposed to the toxemia and the cells suffer some grade of degeneration. Since it is the cells or parenchyma of the viscus which especially suffer, the change in the viscera is commonly called parenchymatous degeneration.

The different infectious diseases show a tendency to affect special tissues and organs. In typhoid fever the muscles suffer; in diphtheria it is the peripheral nerve fibers; in yellow fever, the liver, and in scarlet fever the kidneys. The grade of degeneration depends upon the intensity of the irritant, the cells

showing swelling, granular degeneration, fragmentation, or fatty changes. In the severer forms congestion and a little exudation from the vessels are frequently added to the cellular changes. The function of the organ suffers in a degree corresponding to the grade of degeneration. The cells may recover from the milder forms of degeneration, while necrotic and exfoliated cells are replaced by new ones of the same type.

2. Exudative Inflammation.

Exudative inflammation is marked chiefly by vascular changes and the presence of an exudate of serum, fibrin, pus, and blood. The character of the exudate varies greatly according to the intensity of the irritant and the structure of the tissue.

If the exudate consists largely of serum, the process is termed serous inflammation, if of fibrin it is called fibrinous inflammation, and if of pus, purulent inflammation, etc., with combinations of these types. These grades of inflammation vary principally with the nature of the irritant.

The effects of the inflammatory process depend upon the structure of the tissues.

(a) **In connective tissue** the intracellular substance may be swollen and infiltrated by the exudate. The vessels are congested and all the cells suffer more or less alteration. When the process subsides serum is readily absorbed by blood- and lymph-vessels; fibrin is more slowly liquefied and absorbed; many pus cells may be disintegrated and absorbed, but after an excessive exudate of pus, and much degeneration of cells, a more or less permanent deposit of mucin is apt to be left in the tissue. When an inflammatory process of any type affects the supporting connective tissue of a viscus it is called an interstitial inflammation.

(b) **Mucous Membranes.**—Simple exudative inflammations are often limited to mucous membranes, and are then called catarrhal inflammations.

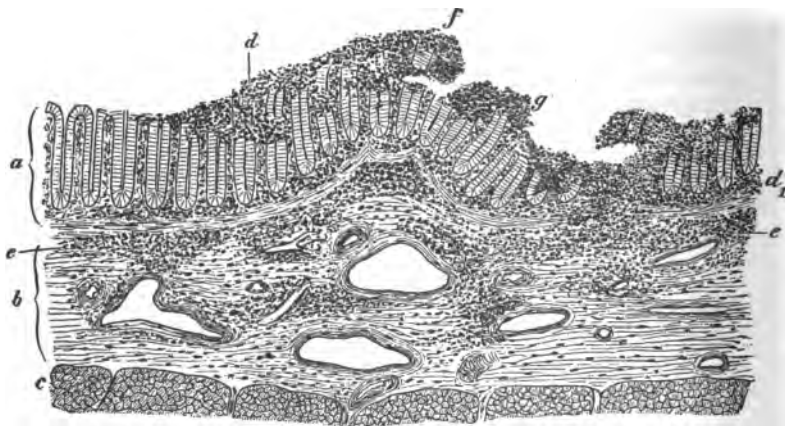
The changes affect (1) the stroma, which is composed of

reticular connective tissue, supporting many lymphocytes, and richly supplied with lymph- and blood-vessels, and (2) the glandular layer, containing glands with epithelial lining.

The stroma suffers the usual changes of exudative inflammation in connective tissue, often varied by the multiplication of lymphocytes.

The glandular layer suffers from the exfoliation of epithelial cells, often leading to superficial erosions or ulcers, which are repaired later by the new growth of epithelial cells. The function of the glands is disturbed. At first the secretion of mucus is inhibited (dry stage); later it is increased and often altered in quality, and at the same time the congestion of the vessels is to some extent relieved. This relation of increased secretion to congestion of a mucous membrane is of importance in thera-

FIG. 21.



DYSENTERY. SUPPURATION AND NECROSIS OF THE MUCOSA OF THE COLON. (Ziegler.)

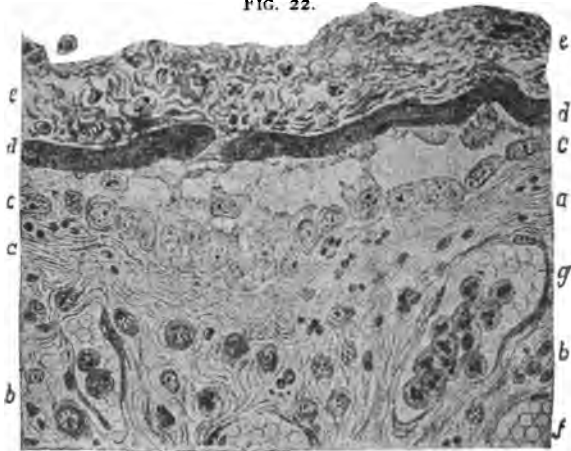
a, mucosa; *b*, submucosa; *c*, muscularis; *d*, *d*₁, infiltration of the inter- and subglandular tissue, *e*, and of the submucosa; *f*, upper glandular layer sloughing off; *g*, ulcer thus produced, its floor infiltrated with leucocytes.

peutics. The duration of the "dry stage" in catarrhal inflammation varies in different mucous membranes, and seems to bear some relation to the amount of lymphoid tissue in the membrane.

Rich fibrinous exudates sometimes form on mucous surfaces and adhere to them as a sort of pseudo-membrane, but without the necrosis of cells which occurs in diphtheritic processes. (*Chronic fibrinous bronchitis.*)

The term croupous inflammation is properly applied to one in which the exudate of fibrin is a prominent feature, but the diversity of usage which this term suffers renders its employment inadvisable.

FIG. 22.



FIBRINOUS PLEURISY. (Ziegler.)

a, b, inflamed pleura; *c*, investing epithelia swollen and exfoliating; *d, e*, exudate of fibrin with serum and pus cells; *f, g*, blood-vessels, containing red cells and polynuclear leucocytes.

(*c*) **Serous Membranes.**—In serous membranes the subserous connective tissue suffers as usual, but the exudate, whether serum, fibrin or pus, is usually poured out in large and often in enormous quantities. Thus a liter of highly albuminous serous fluid is often thrown off by the pleura in a few hours, a layer of fibrin 1 cm. in thickness may form in a few days, while empyema (purulent inflammation) frequently causes such a large exudate of pus that the lung is tightly compressed against the spine. A similar excess of exudate occurs in inflammations of joint cavities, meninges, etc.

(*d*) **Lymphoid Tissue.**—In the lymph nodes and spleen the supporting stroma suffers as usual in exudative inflammation, and there is commonly a pronounced multiplication of lymphocytes, especially about the lymph nodes. The framework of a lymphoid organ is a labyrinthine meshwork in which the strands of reticular tissue are lined by endothelial cells. One of the prominent effects of exudative inflammation is here the exfoliation of large numbers of endothelial cells, often without much exudation, and the process is therefore rightly called catarrhal inflammation. The term catarrhal calls attention especially to the exfoliation of lining cells.

(*e*) **Viscera.**—In the viscera, the stroma may become swollen, edematous, and infiltrated with leucocytes, and these exuded products, usually in small quantity, may be found between the epithelial parenchyma cells, and in the lumen of the alveoli. The cells suffer varying grades of degeneration; their function is interfered with or inhibited; and secreted products are often rendered pathological in character. When the stroma of a viscus is exclusively affected, it is called interstitial inflammation. When the functioning cells are chiefly affected it is called parenchymatous inflammation, and when all parts of the viscus are involved it is called diffuse inflammation. These terms indicate the location but not the grade of inflammation.

3. Necrotic Inflammation.

Intense bacterial or chemical irritants often lead to exudative inflammation with death of considerable portions of tissue, hence the term necrotic inflammation is applied.

In connective tissue, when the exudate compresses blood-vessels and shuts off the blood supply, or when bacterial products exert an intense necrotic action, a portion of tissue dies and is partly liquefied, and an abscess is produced.

In mucous (and serous) membranes and on cutaneous surfaces the same factors lead to the death of a superficial area of tissue, which is readily thrown off as a slough, leaving an ulcer.

The superficial ulcers of catarrhal inflammation are healed by proliferation of epithelial cells, completely restoring the surface, but the deeper ulcers of necrotic inflammation affecting the stroma, are healed by granulation tissue and leave a cicatrix.

In the viscera, abscess, focal necrosis, and death of larger areas of stroma and cells result, healed if at all by granulation tissue and leaving cicatrices. Isolated necrotic epithelium may be replaced by new cells of the same kind.

4. Diphtheritic Inflammation.

Diphtheritic inflammation is the term employed when the process is marked by widespread necrosis, either superficial and involving principally the epithelium, or deeper and extending through the mucosa or even through the submucosa. There is at the same time more or less fibrinous exudate entangling the necrotic elements and adhering firmly to the surface as a false membrane. This process is sometimes called pseudo-membranous, and also, though improperly, croupous inflammation. Now diphtheritic inflammations may not form any false membrane whatever, and simple fibrinous exudates without necrosis may produce abundant pseudo-membrane, so that the three terms—diphtheritic, pseudo-membranous, and croupous—cannot be considered synonymous. It is better to avoid the use of the latter terms altogether, since they do not accurately indicate the grade or type of inflammatory process.

In connective tissues diphtheritic inflammation is not infrequently seen, but is seldom fully recognized, being often classed with spreading suppurative or with gangrenous processes. Here it is marked as usual by diffuse necrosis and liquefaction, or when fibrin is abundantly exuded, by necrosis and coagulation. (*Diphtheritic erysipelas.*)

In mucous membranes diphtheritic inflammation produces widespread necrosis. The depth of the necrotic process varies. If it affects only the epithelium, superficial erosions are produced, usually with much exudate and fully repaired by proliferation of

surrounding intact epithelium. If it attacks the stroma of the mucosa or submucosa true ulcers are formed, healed by granulation tissue and covered over by flat or cuboidal, but not by specialized epithelium. (*Old diphtheritic colitis.*)

If the exuded and necrotic elements are rapidly liquefied no false membrane is produced. (*Malignant diphtheria of the pharynx.*) Usually a membrane is formed as described by the coagulation of the necrotic tissue cells and exuded elements. Such false membranes are usually exfoliated by means of a reactive purulent inflammation in the underlying tissue.

In viscera it is usually difficult to recognize diphtheritic processes from simple necrotic or from gangrenous processes. In the kidney they frequently arise by ascending infection from diphtheritic cystitis.

Types of Ulcers.—Three types of ulcers have been described :

1. From death of lining epithelium only. Such ulcers or erosions result both from catarrhal and from diphtheritic processes, and are usually of small dimensions.

2. From simple necrotic inflammation. Such ulcers involve varying depths of superficial tissues and are usually well circumscribed. (*Syphilis.*)

3. From diphtheritic processes. Such ulcers are of variable depth and are usually of large dimensions.

Many descriptive terms are applied to ulcers, based upon their principal characters, which relate to their

Number and grouping.

Base and secretion.

Edges and vicinity.

5. Productive Inflammation.

Productive inflammation is characterized by the development of new tissue. There may be no accompanying exudation whatever, in which case the process is called simple productive inflammation, or exudation may be added, in productive inflammation with exudation. The latter is much the commoner form.

(a) **Simple Acute Productive Inflammation (Cellular Inflammation).**

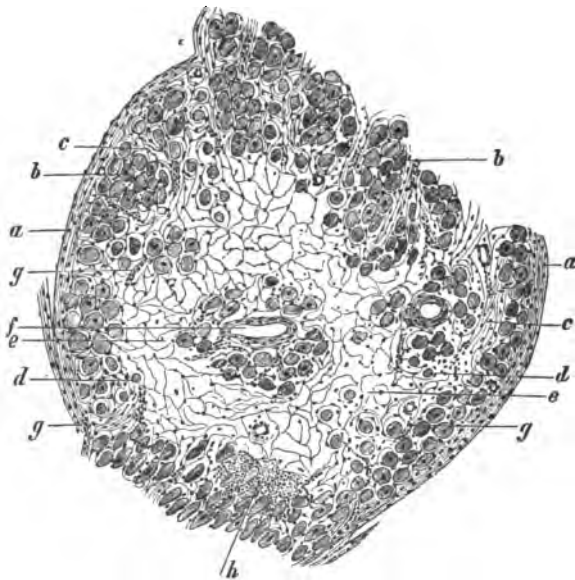
Pure types of this process are rarely encountered, being furnished chiefly by serous membranes, as the peritoneum, pleura, and meninges. The new tissue is composed of new cells formed from fibroblasts and endothelium, while the neighboring vessels are usually in a state of moderate congestion. Owing to the character of the new tissue produced and the absence of vascular changes this process is sometimes called cellular inflammation. Later the new tissue approaches the type of adult fibrous tissue, causing a permanent alteration in the structure of the affected part. The development of a cellular inflammation requires a tissue composed of cells with active proliferating capacities, and an irritant of slow action and moderate intensity. The purest examples have been furnished experimentally, from the application of mild caustics to the peritoneum. It is frequently seen in serous surfaces bounding areas of more intense exudative inflammation, as on the pleura in pneumonia, or on the peritoneal surface of the intestine near the ulcers of typhoid fever.

(b) **Productive Inflammation with Exudation.**

Acute productive inflammation is usually accompanied by vascular changes and by exudation from the vessels. The exudate consists of serum, fibrin, or pus, as in simple exudative inflammation. The new tissue is derived from fibroblasts which are at first numerous and are soon surrounded by delicate intracellular substance. It may contain many mononuclear leucocytes which at this time are indistinguishable from fibroblasts, and it may also be infiltrated with some polynuclear leucocytes. New capillaries are developed from neighboring vessels, but the new tissue is often imperfectly vascularized from the first and prone to various forms of degeneration or even necrosis. (*Tuberculosis, syphilis.*) During recovery the exudate may be removed in the usual way, but the new tissue remains as a per-

manent alteration of the affected part. The final product is usually a dense fibrous tissue.

FIG. 23.



FIBROSIS IN CARDIAC PAPILLARY MUSCLE. (Ziegler.)

a, endocardium; *b*, normal muscle; *c*, fibrous hyperplasia, rich in cells; *d*, atrophic muscle; *e*, fibrous tissue with few nuclei and no muscle cells; *f*, a vein, with a few muscle cells about it; *g*, small blood-vessels; *h*, round-cell infiltration.

It is characteristic of productive inflammations with exudation that they are subacute rather than acute in their course, that their duration is considerable, and that the acute stages are apt to be followed by chronic productive inflammation without exudate. (*Subacute nephritis.*)

The effects of this type of inflammation vary with the structure of the tissue in which it is located.

In connective tissue the exudate infiltrates both the old and the new structures. The new growth adds to the thickness of the old, surrounds and compresses arteries, and forms irregulari-

ties on the surface or adhesions between apposed surfaces. (*Chronic peritonitis.*)

In mucous membranes the exudate infiltrates the stroma, is discharged from the surface, and a catarrhal inflammation of varying intensity is usually established. The new growth is regularly formed in the stroma, which is thickened, obstructs blood- and lymph-vessels, distorts and constricts glands, and causes atrophy of lymphoid cells. (*Bronchitis.*) A mixed exudative and productive inflammation may be limited to the stroma of a mucous membrane with little or no catarrhal affection of the glandular layer. (*Colitis.*)

In the viscera the stroma is the seat of a diffuse new growth replacing the parenchyma of the organ, while the exudate infiltrates the thickened stroma and the epithelial structures and is thrown off with the secretion of the viscus. The parenchyma suffers a variable grade of degeneration and atrophy. The function of the organ is seriously and to some extent permanently impaired. (*Subacute diffuse nephritis with exudation.*)

(c) Chronic Productive Inflammation.

In chronic productive inflammation the new growth is regularly of the type of fibrous tissue. It may at first be comparatively cellular, containing fibroblasts and lymphocytes (round cells), or if of slower formation may have the characters of adult connective tissue, or may finally become densely fibrous. Under some conditions the blood-vessels may be numerous, and the tissue resembles granulation tissue. More often it is imperfectly vascularized, and tends to degenerate and soften or become calcified. (*Endarteritis.*)

There is much controversy regarding the origin of the slow forms of chronic productive inflammation or chronic fibrosis. It appears to be due sometimes to a chronic irritant affecting the stroma of viscera, and at other times it appears to coincide with atrophy and degeneration of the parenchyma cells of the organ. (*Cardiac fibrosis.*)

Chronic productive inflammation may be (1) chronic and continuous from the first, but (2) it usually follows an initial subacute productive process and (3) frequently progresses with marked subacute exacerbations interrupted by periods of partial quiescence. During the exacerbations there may be exudation from the blood-vessels. (*Bronchitis and emphysema, chronic nephritis.*)

In connective tissue thickenings and adhesions are produced and there may be collections of serum, especially when the process affects serous membranes. (*Chronic pleurisy and peritonitis.*)

In mucous membranes the fibrous tissue of the stroma is greatly increased and there may be hyperplasia of lymphoid cells. Polypoid outgrowths often appear, sometimes reaching a considerable size. (*Chronic rhinitis and endometritis.*) Some glands may become atrophic from pressure of the fibrous tissue, or cystic from constriction of their ducts, while the remaining glands may become hypertrophied. In some situations the number and size of the glands may be so much increased as to resemble a true glandular neoplasm. (*Adenomatous endometritis.*) The secretion of the glands may be increased as in the hypertrophic condition in chronic bronchitis, or diminished or absent as in atrophic rhinitis.

In the viscera there is a growth of connective tissue, sometimes infiltrated with round cells, beginning in the stroma and replacing considerable areas of the parenchyma. The blood-vessels are commonly sclerosed and deformed, or obliterated. The parenchyma cells are compressed and atrophic, or exhibit many stages and forms of chronic degeneration. Regenerative efforts on the part of the cells are sometimes a prominent feature. The functions of the viscus are seriously and permanently impaired. (*Cirrhosis of the liver.*)

INFLAMMATION IN BONE.

Owing to the peculiar structure of bone and cartilage inflammatory processes here have some unusual features.

Bony tissue as such is incapable of exhibiting ordinary inflam-

matory changes and the inflammations which affect it are located primarily in the periosteum or the marrow.

It has already been noted that an exudative process of an intensity which would not prove necrotic in other situations may lead to extensive necrosis of bone by occlusion of the nutrient vessels, which, being inclosed in unyielding walls, are soon compressed by exuding serum or pus. Such inflammations are usually located in the periosteum. The dead portion of bone is slowly removed by a reactive inflammation proceeding from the line of demarcation from living bone, by a process which includes in order the following steps:

1. The absorption of calcium salts from a thin layer of bone surrounding the dead bone or sequestrum.
2. The development in this layer of a form of granulation tissue which is capable of exudative changes.
3. The development of a suppurative inflammation in this locality which causes the further absorption and loosening of the sequestrum.

The absorption of bone is accomplished by the blood-vessels and through the instrumentality of certain large giant cells called osteoclasts. The complete extrusion of a large sequestrum is seldom accomplished by natural processes unaided by surgical interference.

When suppurative inflammation affects cancellous bone there is considerable absorption of many trabeculæ, which permits unabsorbed portions to break off in small masses or spicules. This process is called caries.

When chronic inflammation affects bone the common result is the gradual replacement of bony tissue with fibrous tissue, rarefying osteitis. At other times, or at certain points in rarefying bone, the process is chiefly formative, and new bone tissue of a dense variety is laid down. (Sclerosing osteitis. Formative osteitis.) In most of the specific chronic inflammations of bone (gout, rheumatism), both rarefying and sclerosing osteitis go hand in hand, and the shafts and joint surfaces become irregularly eroded and enlarged.

In tuberculosis of bone the changes are usually limited to the absorption and replacement of bone by granulation tissue, which commonly exhibits marked evidence of tuberculous inflammation. In chronic syphilis both rarefying and formative osteitis are often associated.

When chronic inflammation affects periosteum the connective tissues may be thickened but the osteoblasts on the inner surface of the membrane usually multiply and lay down irregular laminæ of new bone, causing deformities of the surface (inflammatory exostoses). These exostoses often grow to a large size and may be mistaken for tumors of bone.

When inflammation of any type affects the marrow of bone the process is called osteomyelitis. In the marrow the changes produced are similar to those occurring in other lymphoid tissues, while the effects upon surrounding bony structures are similar to those resulting from periostitis.

CHAPTER VII.

NEOPLASMS.

A SPONTANEOUS, relatively functionless, progressive, non-inflammatory development of new cells, more or less circumscribed, is called a neoplasm, and when it is specially marked by swelling, a tumor; excluded from this definition are all collections of blood and inflammatory products and excessive development of a functioning part. If the tumor reproduces tissue which is normal in the organism it is said to be typical; if new or embryonic tissue, it is called atypical. Neoplasms are sometimes grouped according to their effect upon the patient as benign, when but little general damage is done, and malignant when the tumor tends to spread and cause profound constitutional disturbance. They are also classed according to the type of tissue in them or from which they have developed, and in the absence of more light on the subject this latter method, the histogenetic, is the most reasonable.

Several theories have been offered to account for the development of tumors, namely that a portion of an embryonic tissue has been included in some other tissue and remains there until an exciting cause, as local injury, excites it to develop; injury without such foci of included germinal tissue, and superficial irritation; infection by parasites peculiar to each kind of tumor. None of these holds for all varieties of tumors and the parasitic origin is generally received only for the so-called infectious granulomata. Certain predisposing conditions are supposed to favor tumor growth, and heredity has been emphasized in the case of malignant tumors especially. Some tumors occur most frequently before adult age is attained, others afterward.

In external form tumors may be circumscribed, the new growth being contained in a fibrous capsule, or they may be infiltrating; the main histological distinction between them is that the former grow centrally and the latter along the periphery, and clinically the latter are the more malignant. Tumors are said to be primary when first formed in a tissue, and secondary when occurring afterward elsewhere; they propagate directly along the continuity of the tissue; or by contiguity, as when a tumor of the uterus involves the intestine because that happens to lie against it; or by metastasis. Metastasis is the name given to the actual transportation of cells from the primary tumor to some other point, as when cancer of the cervix uteri is repeated in the breast or the lung. These cells pass through either the lymphatics or the blood-vessels. Carcinoma of the stomach may ulcerate, open venous radicles and cause thrombosis, from this malignant thrombosis emboli carried to the liver set up similar neoplasms where they lodge. Carcinoma mammæ is usually transported through the lymph circulation, or directly through the chest wall. Often, however, the neoplasm grows along lymphatic passages in a direction contrary to the lymph stream, the cells proliferating from the end of the neoplastic column in the line of least resistance, and also laterally, distending the channel.

The structure of tumors may be like that of any tissue in the body and may be made up of muscle, fibrous tissue or gland cells which elsewhere would be taken for normal; or they may contain chiefly cells which are normal only in the embryo; their blood-vessels are either like the normal or mere channels hollowed out through the substance of the new growth; nerves have been found in some forms other than those developed in nervous tissue. When a tissue develops other than in its normal place it is called heterotopous; forming at a life period when it does not normally occur it is termed heterochronous. Tumor cells may deserve either or both of these adjectives.

In the microscopic diagnosis of tumors it is important to decide first if the tumor reproduces normal tissue; if not, then

the relation between the stroma and the cells is of special significance ; if a basement substance is made out between the cells it speaks for a diagnosis of sarcoma ; if epithelial cells are found in groups (which are of course sections of long bundles or columns) without glandular arrangement or simulating gland acini, the probability is that the tumor is carcinomatous. The derivation of the new tissue is also of great importance, but in the atypical neoplasms the question is not always easy to decide. Microscopic examination of the edge of the tumor, where its cells are youngest, is often necessary to determine their origin. The more one type of tissue prevails the greater the probability that the tumor should bear the corresponding name, but mixed tumors may occur which in one portion resemble one type and in different portions another.

If localized and benign, the effects of a tumor may be merely inconvenience, pressure and dragging excepted. When malignant the general condition suffers from poisonous products, from invasion of important organs and the resulting disturbance of function, from pain, and from inflammatory changes in and about the new growths. Malignancy in the ordinary use of the term refers especially to the sarcomas and the carcinomas. Clinically the term includes multiplication of the tumor as well as local increase, and all the features of the cachexia. Histologically the diagnosis depends upon the destruction of natural boundaries by the rapidly proliferating cells, which are apt to have large vesicular nuclei and to show acidophile characters whether they come from fibroblasts or epithelia. In proportion to their malignancy they return to the "embryonic" condition, in which their chief occupation was to multiply, and give up the functions of later acquisition ; that is, the "habit of work" characteristic of the adult specialized cell is lost and only the accelerated "habit of growth" persists. Hence they do not pause in their multiplication and older cells are unable to resist them. The less this is noticeable the less malignant is the tumor. Many tumors present various forms of degeneration in

their cells, usually in the older portions, as colloid, mucoid, etc. Occasionally a benign tumor becomes malignant by such changes, as when a subserous uterine myoma becomes twisted on its pedicle and undergoes necrotic softening from loss of nutrition; the fluid contents may escape and set up peritonitis.

A tumor is named by adding to syllables indicating the tissue it resembles, the syllables -oma, which have been agreed upon as equivalent to tumor; in the case of sarcoma and carcinoma these words are retained entire with the tissue name prefixed.

Classification of Tumors.

A, I.—CONNECTIVE TISSUE TUMORS—SIMPLE.

NORMAL TYPE.	TYPICAL TUMOR.	ATYPICAL TUMOR.
I. Connective.		
1. Fibrillary.	Fibroma, hard and soft.	Fibro-sarcoma (desmoid)
2. Wharton's jelly.	Myxoma.	Myxo-sarcoma.
3. Fatty.	Lipoma.	Lipo-sarcoma.
4. Cartilage.	Chondroma.	Chondro-sarcoma.
5. Bone forming.	Ossifying fibroma.	Osteoid sarcoma (osteoblastoma).
6. Bone.	Osteoma.	Osteo-sarcoma (chondro-osteosarcoma).
II. Vascular.		
7. Arteries.	Arterial angioma.	Plexiform angioma.
8. Veins.	Cavernous angioma.	Cavernous angiosarcoma.
9. Embryonic vessels.	Nævus vasculosus.	
10. Lymph vessels.	Lymphangioma cysticum and cavernosum.	
III. Muscle and Nerve.		
11. Smooth and striated muscle	Leiomyoma and rhabdomyoma	Myo-sarcoma; myogenic spindle-celled sarcoma.
12. Embryonic muscle.		
13. Nerve, peripheral and central.	Neuroma verum; neuroganglioma.	Neuroma malignum (?).
IV. Connective tissue, rich in cells.		
14. Lymphatic.	Lymphoma, lymphadenoma.	Lymphosarcoma; myeloma.
15. Neuroglia.	Glioma.	Glio-sarcoma.

- | | | |
|---------------------|----------------------------|--------------------------|
| 16. Endothelium. | Lymphangioma endotheliale. | Alveolar endothelioma. |
| | Perithelioma. | Fasciculate endothelioma |
| 17. Pigment tissue. | Pigmented mole. | Melano-sarcoma. |
- V. Placental.
- | | | |
|------------------------|-----------------------------|--|
| 18. Decidua syncytium. | Simple deciduoma. | Malignant deciduoma. |
| 19. Chorion. | Placental polyp. | |
| | Simple mole, myxoma chorii. | Destructive mole, myxo-sarcoma chorii. |

A, 2.—CONNECTIVE TISSUE TUMORS—COMPOUND.

- | | | |
|----|-----------------|--------------------------|
| 1. | Chondrofibroma. | |
| 2. | Myxolipoma. | Corresponding sarcomata. |
| 3. | Fibromyoma. | |
| 4. | Angiomelanoma. | |

B.—EPITHELIAL TUMORS.

- | NORMAL TYPE. | TYPICAL TUMOR. | ATYPICAL TUMOR. |
|--------------|----------------|-----------------|
|--------------|----------------|-----------------|
- I. Surface epithelium.
- | | | |
|---|--|--|
| 1. Of skin, mucous membranes and papillæ of same. | Simple epithelioma, Keratoma (Horns), Hard papilloma (larynx). | Flat celled carcinoma. Carcinoma of mucous membranes covered by squamous epithelium. |
| 2. Transitional and Cylindric. | Papilloma cylindrocellulare (stomach, gut). | Cylindric celled carcinoma; papillary carcinoma of mucous surfaces. |
| 3. Ciliated. | Papillary cystoma (ovary). | Papillary ovarian carcinoma. |
- II. Glandular.
- | | | |
|--|--|---|
| 4. Of tubular type (sweat, kidney). | Tubular adenoma (sweat glands, alimentary canal). | Adeno-carcinoma: glandular carcinoma in various glands with atypical alveoli. |
| 5. Of acinous type (breast, salivary). | Alveolar adenoma (mucous glands, breast, thyroid gland). | |
| 6. Of follicular type (thyroid gland). | Adeno-cystoma (ovary). | Adeno-cysto-carcinoma (ovary). |
| 7. Adrenal. | Hypernephroma. | Malignant hypernephroma. |

C.—MIXED TUMORS—TERATOMATA.

1. Typical tumors arising from inclusion of one or more embryonic layers.
- Dermoid cyst, part of ectoderm caught during infolding; tumor contains skin, hair, cutaneous glands.
 - Cysts from cylindrical and ciliated epithelium; enterocystoma; branchiogenic cyst.

2. Mixed tumors arising from scattered parts of the germinal layers.
 - a. Combinations of typical connective and gland tissue ; fibro-adenoma, chondro-adenoma.
 - b. Combined atypical gland and connective tissue ; adenosarcoma ; adeno-chondro-sarcoma ; carcinoma sarcomatosum.
3. Mixed tumors representing rudimentary development of an embryonic layer (embryoma).
 - a. Compound dermoid cyst of testis and ovary ; parthenogenetic embryoma.
 - b. Inclusion of rudimentary fetus in body cavity of a twin ; fetus in fetu ; parasitic embryoma.

A. Simple Connective Tissue Tumors.

Fibroma.—Consists wholly of connective tissue with its vessels ; of two forms, hard and soft—the former resembling areolar tissue, the latter made up of bundles of fibrous tissue woven tightly together. Soft fibromata are usually round, lobulated, may be enormous, develop in skin and subcutaneous tissue and leave the skin wrinkled after they atrophy ; may be pigmented and multiple ; occur also from fascia, bone and retroperitoneal tissue.

Combinations, lipoma, myxoma, chondroma, sarcoma.

Hard fibroma ; usually circumscribed, round, firm and tough, surface white and smooth on section, with concentric arrangement of fibers ; grows slowly, may be multiple.

Occurs in fascia, periosteum, gland capsules, nerve sheaths. Combinations, myoma (frequent in uterus), cyst formation by softening, sarcoma.

Microscopic.—Soft ; fibrous or homogeneous connective tissue with vessels, in large and fine mesh work, spaces filled with serous or mucous fluid. Hard ; fibrous tissue in closely packed bundles, homogeneous or fibrillary, small collections of cells here and there, corpora amylacea frequent ; veins may be irregularly dilated, like angioma.

Keloid.—A variety of fibrous new growth developing in the corium and presenting on the surface as small nodules and ridges. They have been called cicatricial when connected with a scar,

and true keloid when spontaneous, but as a matter of fact they develop from injury always and are never spontaneous. Even a trivial injury will serve as a starting point in a patient who is disposed. They begin by proliferation of the fibroblasts along the small vessels, and reach deeply inward along their course as well as appearing on the surface. They differ from a cicatrix in always exceeding the limits of the wound, whereas a scar, even if hypertrophied, remains localized—is not a neoplasm, in other words.

Myxoma.—Usually round or lobulated, encapsuled or not, feel semifluid on palpation; section grayish, viscid, with fibrous bundles. *Microscopic*, basement substance mucous with round, stellar or spindle cells connected with each other by their poles; acetic acid precipitates mucin in fine reticular form. Occur in sheaths of nerves and tendons, from fatty tissue, degenerated fibroma, and as polyps in nose and pharynx.

Combinations, of especial clinical importance, with sarcoma.

Glioma.—Usually single, of slow growth from neuroglia, on reaching dura does not extend into it; from small focus to size of fist, grayish or yellowish, fairly firm. *Microscopically* contains round, spindle or multi-polar cells, may be bundles of fibrous tissue, vessels few or many, in last case frequent hemorrhages, may soften and become cystic.

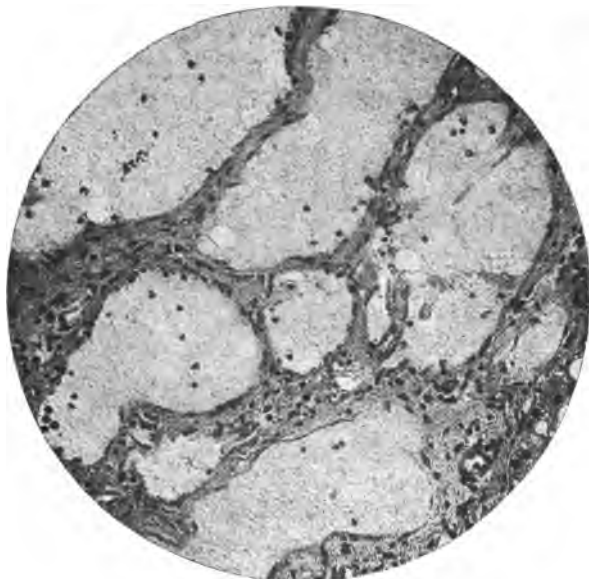
Lipoma.—Roundish, lobulated, may be capsuled, soft but not fluctuating; on section areas of fat marked out by fibrous bundles clearly demonstrated; both the fat cells and the tumor lobules are larger than normal and not uniform in size; otherwise reproduces fat tissue; from overgrowth of normal fat or metaplasia of connective tissue; growth slow; in subcutaneous tissue, in joints, in fascia, may occur or persist in the emaciated.

Chondroma.—May contain any kind of cartilage; called enchondroma if found in abnormal place as in testis, ecchondrosis if growing from cartilage and small. Usually hard, circumscribed, may reach large size; on section firm and homogeneous or hard and marked by fibrous bands; degenerates easily, forming cysts, or contains lime salts in quantity.

Combinations ; lipoma, fibroma, myxoma, sarcoma.

Osteoma.—Bone tumors occur from inflammatory processes in the periosteum or as hypertrophies of normal bone, or in combination with other tumors. They are called osteophytes if small ; flat, superficial deposits ; exostoses if more localized, round and spur-like ; parosteal osteomata if developed apart from bone.

FIG. 24.



CAVERNOUS ANGIOMA OF THE LIVER. (PHOTO.)

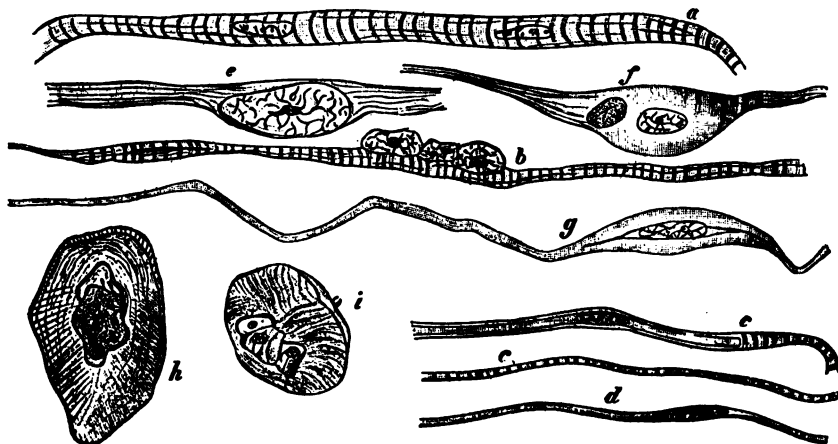
Large irregular blood channels surrounded by compressed fibrous and hepatic tissue containing atrophic cells.

The name osteoma is applied to bone tumors which are circumscribed, of steady growth, and made up of spongy or compact new bone tissue. Three forms are described, osteoma durum, spongiosum and medullosum, according as they are of hard bone, of spongy with a few marrow spaces, or with much marrow.

Occur from bones, at times after injury, cartilage, and fibrous tissues as pleura and diaphragm. Benign and of slow growth.

Hemangioma.—Consist of a small amount of connective tissue and great disproportion of vessels, newly formed and hence excluding varix and aneurysm; may increase in volume on stimulus and then called erectile. Three varieties: telangiectatic, hemangioma simplex, or nevus, consisting of dilated capillaries; hemangioma arteriale plexiforme, of tortuous thick-walled arteries; and cavernous, like corpus cavernosum penis in structure.

FIG. 25.



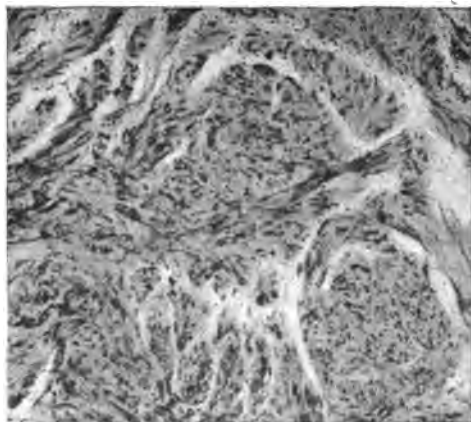
CELLS FROM RHABDOMYOMA. (Ziegler.)

a, b, c, striated muscle cells of varying thickness; *d*, slender smooth muscle cell, with nucleus; *e*, spindle cell, striæ longitudinal; *f*, spindle cell, striæ transverse; *g*, spindle cell with long processes, no striæ; *h, i*, round cells, striæ radiate or concentric.

Myoma.—Tumors of striated muscle cells are called rhabdomyomata and are among the most uncommon. Those of smooth muscle tissue are called leiomyomata and occur in the uterus, intestinal canal, prostate and skin. They may be cystic or cal-cified, are usually of slow growth and benign.

Combination with fibroma common.

FIG. 26.



LEIOMYOMA OF THE UTERUS. (PHOTO.)

Islands of muscle fibers mapped out by light bands of fibrous tissue.

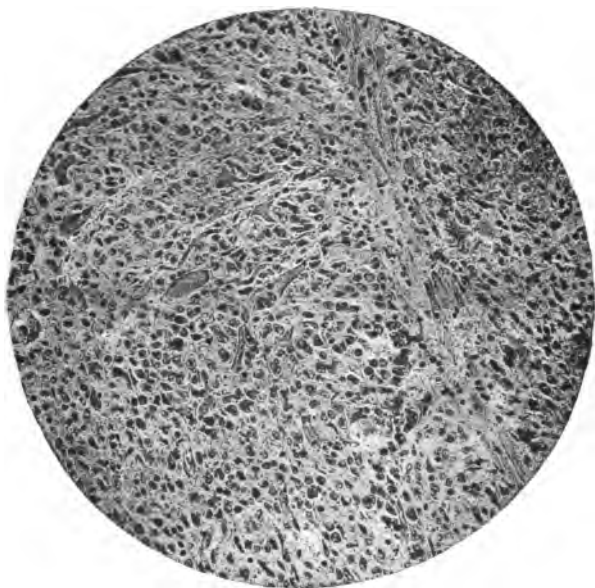
B. Tumors from Connective Tissue with Excessive Cell Formation.

Sarcoma.—Tumors developed from connective tissue, with the stroma disproportionately sparse and the cell formation excessive and tending to progress, the cells having an embryonic or imperfectly formed character, are called sarcomata.

Sarcoma may develop from any of the tissues grouped under the name of connective, and often retains analogies with the special kind from which it is developed; thus sarcoma in the choroid tunic of the eye often forms pigment, and in the periosteum, bone. The relation to connective tissue may be recognized also in the fact that the tumor cells are closely connected with each other and even when most richly present tend to form fine intercellular substance, which can be demonstrated by proper staining methods. In one sense, then, we may speak of the stroma and the parenchyma of such tumors. The commonest forms of cell formation found in them are the round, resembling

lymph cells or exceeding them in size, the spindle form of varying sizes, star-shaped, and giant cells. The intercellular sub-

FIG. 27.



SMALL ROUND-CELLED SARCOMA. (PHOTO.)

stance is either fibrillary, granular, homogeneous or reticular and varies within wide limits in proportion to the cells. It may be so scanty that special stains (as Van Gieson's) and the higher powers of the microscope are required to recognize it. The vessels may be so many and large that the tumor is cavernous, and most often a peculiar relation between vessel wall and cells may be recognized; the cells are closely applied to the vessel with only faint indications of a wall, or the blood channels are simply tunneled through the tissue; hemorrhage from sarcoma vessels is common.

Varieties. The kind of cells predominating determines the kind of sarcoma :

FIG. 28.



LARGE ROUND-CELLED SARCOMA.

1. *Round-celled sarcoma* may be of either the small- or the large-celled variety ; the small-celled resemble granulation tissue and have but little stroma. In the gross they are soft, the cut section gives a milky juice on scraping ; they grow rapidly, are not encapsuled, form many and early metastases and are among the most malignant ; from connective tissue of muscle, fascia, bone, testis, brain, etc. Large round-celled sarcoma differs chiefly in the size of the cells and the occasional alveolar arrangement. These cells

are derived from fibroblasts. They are called large round cells but their actual outline is quite as often polygonal.

2. *Spindle-celled sarcoma*, also divided into large- and small-celled, one of the commonest sarcomas; resemble muscle cells if large; may lie closely packed or appear as a fibrillar stroma between bundles of spindle cells.

FIG. 29.



FIBRO-SARCOMA. (PHOTO.)

3. *Giant-celled Sarcoma*.—The main tumor may be of any kind, but with the other cells there occur giant cells, large spheres of protoplasm with many centrally grouped nuclei, often oval shaped. Such giant cells are commonest in sarcoma developing from periosteum and bone. In the giant cells of the

infectious granulomata and those formed about foreign bodies the nuclei may be arranged as a crescent at one pole of the cell or as a complete peripheral ring. Their longer axes may coincide with the radii of the cell. This type is known as the Langerhans giant cell and is distinguished from the myeloid, whose nuclei are central.

Grouped according to the variety of the connective tissue which forms their foundation and origin, sarcomas are described as :

Fibro-sarcoma,
Myxo sarcoma,
Glio-sarcoma,
Chondro-sarcoma,
Osteo-sarcoma,
Melano-sarcoma,
Myeloid sarcoma,
Lympho-sarcoma,
Myo-sarcoma,
Neuro-sarcoma,
Angio-sarcoma.

These tumors grow rapidly in proportion to their cell contents and the size of the distinguishing cells ; of all, the small round-celled most quickly. Their nutrition, because of the many and relatively large vessels and their relations, is very free. Fibro-sarcoma may be encapsuled, other varieties seldom, but even with a capsule the tumor grows through and beyond it, increasing peripherally, pushing between other elements and replacing other tissues. The very cells of the capsule themselves become sarcomatous. They may remain stationary for a time and then suddenly increase in size or grow rapidly to large size from the start. They are very prone to degenerate, hence every form of necrotic and softened area and consequent cystic formation may occur. On the surface of the body they break down and form

ulcers. When a hyaline degeneration involves the blood channels, converting them into swollen cords and decreasing their lumen, the tumor is called a cylindroma. When modified fat pigment gives the tumor a green color it is termed chloroma.

FIG. 30.



ANGIO-SARCOMA. (PHOTO.)

A tumor of this type has always been called angiosarcoma; a better name perhaps would be angio-endothelioma.

Their malignancy is seen in their rapid growth and invasion of parts directly, frequent metastasis (most often through the blood-vessels), and prompt recurrence after operative removal. Constitutional depression is not so marked as in carcinoma. With multiple metastases all through the body the dissemination is spoken of as a sarcomatosis, as the similar condition in cancer is called carcinomatosis.

The etiology is more clearly dependent upon late development of fetal remnants than in the case of some other tumors; to which opinion the occurrence of congenital sarcoma, and the development of simple and complex sarcomas of the testis,

FIG. 31.



ENDOTHELIOMA OF PLEURA. (Ziegler.)

a, fibrous stroma; *b*, endothelial cells proliferating along lymph spaces in strands and columns.

parotid gland and thyroid, of heterotopous nature lend probability.

Endothelioma.—Proliferation of endothelial cells is comparatively common in some tumors, at times collected in heaps and bundles, sharply marked off from the stroma. Such tumors have been grouped with carcinoma and then with sarcoma, but in carcinoma the relation between the epithelium of the tumor and the epithelium of the tissue of origin is demonstrable, and the

relation of the cells of a column in a lymph space to the wall of the space is so loose that they retract from it in hardening; while in endothelioma the cells are organically connected with the intercellular stroma derived from them, and in the case of many endotheliomas the derivation of the cells from the endothelial cells of the part has been observed. The endothelial tumors appear to belong to the connective-tissue group because of the fact of frequent transition and combination forms between them and both the typical and the atypical tumors of this class. Possibly the same stimuli which cause the endothelia to proliferate produce like effect upon the fibroblasts of the part, or conversely. Quite frequently endothelioma begins in the finer lymph spaces of connective tissue or in the walls of lymph channels. These tumors occur in several forms, namely, interfascicular, plexiform, perivascular, diffuse and alveolar. These forms are chiefly dependent upon the nature of the tissue in which the endothelial proliferation starts, especially with reference to the lymph spaces. If made up of firm fibrous bands, running chiefly parallel, the lymph channels and radicles have the same general disposition, and the new cells make their way along them and form the fascicular type. Here lines of single cuboid cells lie in long narrow spaces, often more than a hundred, one behind another, the terminal cells at each end being longer. Where the lymph spaces form a close network, with fine or coarse meshes, the tumor is plexiform. When cell multiplication is rapid and pressure but slight, the walls of the spaces are pressed apart and the alveolar type is assumed. The other names are self-explanatory. Endotheliomas have been found in the cerebral membranes, marrow, testis, ovary, lymph nodes, etc.

A special form of endothelioma occurs as a superficial thickening of serous membranes, or as little spheroids scattered over them, and may strongly resemble such membranes when thickened by chronic inflammation; metastasis may occur in the lung, liver, muscles, and elsewhere.

Tumors Resembling Sarcomata. Syncytioma, Mixed Forms.

Syncytioma or Deciduoma.—Simple and malignant tumors may develop from the decidua after interrupted and normal pregnancies, immediately or after long intervals of time. Many are of rapid growth, degenerate easily, form metastases in vagina and lung especially, and are extremely malignant. Three forms of cells are found; large epithelioid, with nuclei rich in chromatin, arranged in network with wide blood spaces between; small, polyhedral, rich in glycogen, in masses between the other kind; and all transitions between these.

Mixed Forms.—Mixed sarcomatous tumors occur in the parotid and thyroid glands, in the ovary and the testis, and contain mucous, vascular, cartilaginous and other elements; they may be referred to inclusions at the point of origin of embryonic cells already differentiated, which are held in an undeveloped condition till some stimulus causes them to form tumors.

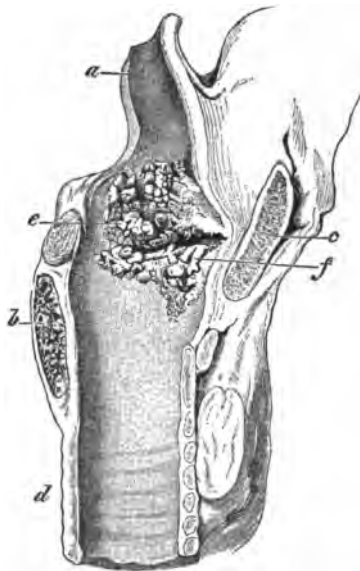
C. Tumors of the Type of Superficial Epithelium.

Simple hypertrophy of the epidermis may occur as the result of repeated slight irritation. Apart from such growth there are several forms covered by the name papilloma, verruca, condyloma, etc.

Papilloma.—This is made up of connective tissue and its vessels and is covered by a single or multiple layer of epithelial cells, and the physiological type is found in the papillæ of the skin and the villi of the intestine. The variety of the epithelial covering differs with the site of origin and attachment of the tumor; the vessels may be divided into loops corresponding each to a subdivision of the tumor or they may form networks of great complexity; the whole may be compared to a tree of connective tissue with frequent branches, which vary much in size and are clothed with a layer or two of epithelium; some-

times the normal papillæ seem merely to enlarge, at others they branch as stated. In the gross there may be countless small tumors, or one or two mounted on pedicles, or a small area covered with the fine subdivisions on a common base; the color and density depend upon the thickness of the epithelial

FIG. 32.



PAPILLOMA OF LARYNX. (Ziegler.)

a, epiglottis; *b*, cricoid cartilage; *c*, hyoid bone; *d*, trachea; *e*, false vocal cord; *f*, true vocal cord, both bearing papillary outgrowths. Between them is the opening of the sinus of Morgagni.

layer, the amount and kind of connective tissue and the richness in vessels. Papillomata are divided into the hard, embracing those of the skin covered with cornified epidermic scales and of the mucous surfaces covered with pavement cells, and the soft which are often covered with modified cylindrical (ovoid) epithelium and are found in hollow viscera. Common examples

of the hard papilloma are the warts found on the fingers about puberty, cornu cutaneum, and pointed condylomata (the latter seem at times to be contagious, both in man and the lower animals). Soft papillomata have a stroma richer in cells and vessels than the hard and seldom present horny epithelia on the surface, the usual covering is that of the part where they grow, though cylindric cells may be found in papilloma developed among squamous. They occur frequently in the bladder, rectum, uterus and vagina, less often in the breast (ducts), gall-bladder and ependyma of brain ventricles; combinations with carcinoma are found. They are dangerous because of their tendency to bleed.

D. Tumors of the Type of Gland Epithelium. Adenomata.

Transitions from enlarged glands to adenomata are frequent and hard to define, and on the other side the adenomata fade into the true carcinomas. Adenoma may be defined as an independent new formation reproducing typical glandular tissue, made up of connective tissue arranged about spaces which are lined by epithelium. While these epithelia are not strictly functionless—for no living cell can be so regarded—yet as concerns the organism they probably do not aid in constructive metabolism. Adenoma may usually be recognized by the unaided eye, by its different appearance from normal gland and by its circumscribed form, often being encapsuled by fibrous tissue; the picture of the hypertrophy of functioning glands, as breast and kidney, is a very different one, as also of glands swollen by confined products.

Adenomas developing in gland or from scattered fragments of embryonic tissues will usually be found encapsuled, seldom diffuse, and on surfaces are usually broad or polypoid. Two types are found according to the prevalence of tubular or acinous arrangement of the alveoli; the former on mucous surfaces and in the ovary, the latter in the breast: the adjective heterotopous is applied to adenoma which develops apart from normal glands or in glands but of abnormal type, as a papillary adenoma in the kid-

ney which does not correspond with renal structure. Adenoma may arise from embryonic fragments which develop wrongly later, or from misdirected repair and hypertrophy after inflammations; the latter form leads directly to carcinoma in some cases. Certain of the primary carcinomas of the liver may be thus explained.

FIG. 33.



ADENOMA OF THYROID. (PHOTO.)

The main distinction between adenoma and carcinoma is found in the typical character of the former as contrasted with the atypical alveoli of the latter, although as compared with normal gland the adenoma is not physiological; thus in glands of acinous structure we may find the adenoma developing tubular glands, and instead of a single layer of epithelium there may be two or more, perhaps cuboid and with papillary outgrowths. But in contrast with carcinoma, the new-formed cells lie in actual gland

spaces and are distinctly separated from the basement substance, often by a membrana propria.

The usual degenerations, fatty, mucoid, and colloid, may occur in adenoma, and hence the tumor can be cystic; by the pressure exerted thus from within, the walls of adjoining spaces disappear and thus the tumor becomes lobulated (adenocystoma).

Though usually benign, except for mechanical effects, adenomata may break into blood and lymph channels and cause metastasis, and especially in the alimentary canal they develop at

FIG. 34.



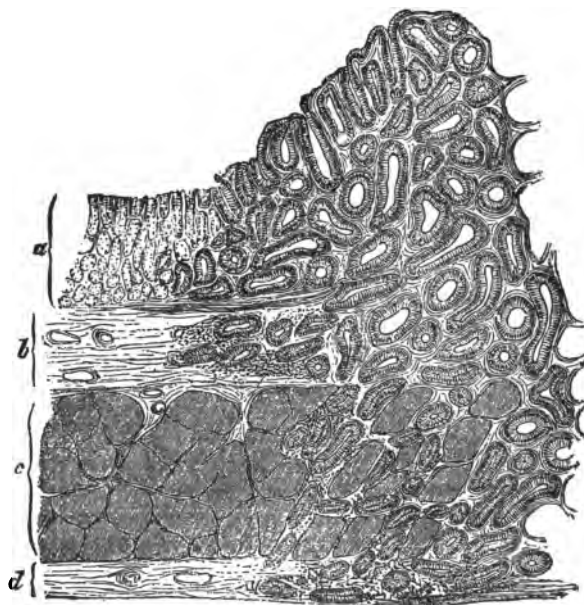
ADENOMA DESTRUENS. (PHOTO.)

A cellular stroma enclosing gland acini which are lined by several layers of epithelial cells. Both acini and epithelia are atypical, but the cells do not transgress the limits of the acini and invade the stroma.

the expense of the submucous tissues, grow rapidly and are clearly malignant (adenoma destruens of stomach, gut and

uterus). Such a tumor may be considered as an adenoma which has become carcinomatous. Combination with sarcoma is also

FIG. 35.



MARGIN OF AN ADENO-CARCINOMA. (Ziegler.)

a, mucosa; *b*, submucosa; *c*, muscularis; *d*, serosa; *e*, neoplasm starting in the mucosa and invading all the other coats. Diagrammatic.

found; here it is the stroma which is especially affected by the cellular hyperplasia.

Hypernephroma.—Occasionally adenomas develop in the abdominal organs, especially kidney, liver, and internal genitals (broad ligament), which reproduce the structure of the adrenals; they are evidently due to the late development of scattered portions of adrenal tissue, which have been found in the abdominal sympathetic ganglia also.

E. Atypical Epithelial Tumors.

Carcinomata are neoplasms made up of connective and epithelial tissues arranged atypically, the latter often multiplying by atypical mitosis and always having a tendency to transgress normal tissue-limits.

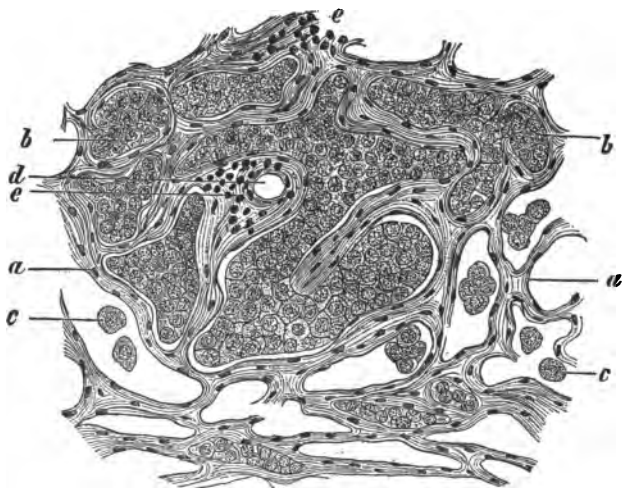
The cells in this group of tumors are the characteristic element rather than the stroma, and still it must be remembered that there is no uniform cancer cell—no cell which apart from its environment would always be demonstrable as a cancer cell. Yet in their usual sites of growth they may be at once recognized. From their resemblance to normal epithelia they are called epithelioid. They may be many times larger than any normal epithelial cell; their nuclei may be large and vesicular and stain so intensely that it is evident that their chromatin differs from that of the normal cell, a condition known as hyperchromatosis. They may multiply by atypical mitosis, showing tripolar and multipolar forms and irregular or superfluous monasters and diasters. These two characters are related to their extremely rapid proliferation, which in turn is one of the elements of their malignancy. When rapidly formed in a part where they are not subjected to much pressure the cells may be small and round, the protoplasm in relatively small amount. By mutual pressure they take on polygonal outlines, and compressed by firm fibrous tissue they may have one axis much longer than the others. Under some pressure conditions, or when the nuclei multiply at a faster rate than the protoplasm, giant cells occur.

In apparently normal glands where the cells are beginning to take on the atypical character, often the first observed variation from the normal is their rapid proliferation, the acinus being then lined, it may be only at one point, by a double or triple layer of epithelia.

Tumors of this group exhibit many variations in form, consistence, gross appearance and anatomical relations; they may be very hard if containing much fibrous stroma (scirrhus), or

soft and resembling brain tissue when very rich in cells (medullary). According to such circumstances and the kind and size of the cells, the microscopic picture also is varied; the framework of the tumor is made up of new connective tissue, and

FIG. 36.



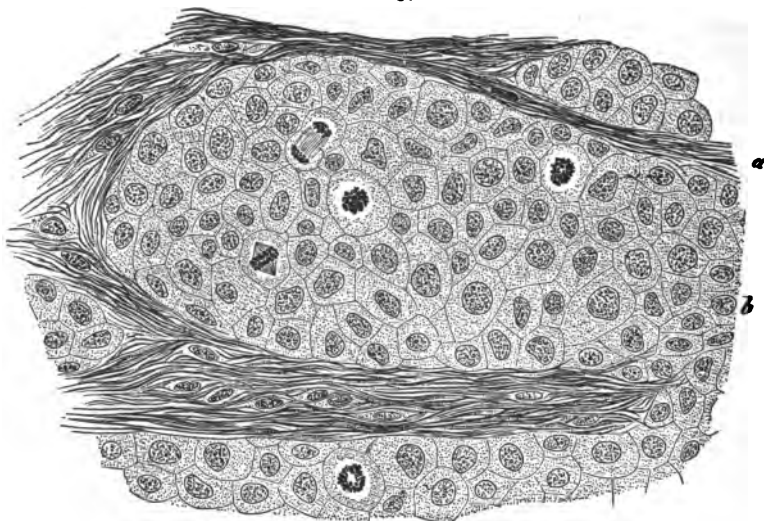
CARCINOMA SIMPLEX. (Ziegler.)

a, fibrous stroma; *b*, cylinders of cancer cells cut at various angles; *c*, single epithelioid cells; *d*, blood vessel surrounded by fibrous tissue; *e*, round cells.

mingled with it, unlike any normal adult tissue, are groups and strands of epithelia, arranged in solid bundles or lining alveoli in one or several layers. The form of the cells depends upon the tissue of origin, those in superficial cancer of the skin resembling epidermis cells, those from the primary carcinomas of the liver copying the liver cells or the epithelia of the bile capillaries; and after the tumor has developed there is a polymorphism of the cells which carries them much farther from the normal; if rich in protoplasm, they are soft and easily altered by pressure, so that round, spindle, polygonal and irregular cells at times coexist in the same part. Further, as degenerative

changes are common, these also modify the appearance of the cells.

FIG. 37.



CARCINOMA MAMMÆ. (Ziegler.)

a, fibrous trabeculae; *b*, large atypical epithelia of polygonal outline, showing mitotic figures.

The stroma may be partly derived from the region in which the tumor develops and in greater part from new connective tissue; occasionally muscle, fat, or gland tissue remains in the tumor for a time. All varieties of stroma are found, from young granulation tissue, rich in cells, to spindle-celled and fibrous; it grows with less energy than the epithelial cells and presents few mitotic figures. Plasma cells also are found and when the tumor suffers the changes due to irritation and inflammation, lymphocytes and polynuclear leucocytes occur. In carcinoma connected with bone, plates of ossification may be found and giant cells as in sarcomata.

The relation of the tumor to the neighborhood in which it grows varies with the rapidity of its growth, and that varies with

the kind of cells present and the amount of stroma ; but all such tumors infiltrate neighboring tissues by extremely fine peripheral processes, so that the apparent gross limit of the tumor is often not the real edge of the neoplasm and in operative removal there is danger of leaving behind small foci from which the tumor will

FIG. 38.



COLLOID CARCINOMA. (PHOTO.)

develop anew. Thus in cancer of the breast the skin may be interruptedly involved, and present minute nests of embryonic epithelia at a distance from the main tumor. These foci, at times hardly visible in the gross, are the starting points for recurrent tumors. They may have spread laterally through the cutaneous lymph channels ; but the skin may become involved from below also, lines of proliferating cancer cells from a more deeply seated tumor following lymphatics against the stream.

Slowly growing carcinoma is apt to be fibrous, hard to the touch, and as the fibrous tissue contracts it dimples the surface, as in some carcinomas of the breast. Beside the local growth, metastasis is common by way of the lymph channels, and at times through the blood-vessels also. The secondary tumors so formed usually reproduce the character of the primary.

Degenerative changes are more common than in normal epithelium, but while the center or the surface may degenerate the tumor persists in its peripheral development and only as an exception is the regressive change a healing process. Either the stroma or the cells may degenerate, and there is an apparent correspondence between such changes and the part where the tumor occurs; breast cancer often becomes fatty, in the mucous tissues mucoid change is common, and in the thyroid, colloid. Such a relation seems to point to a partial conservation of the function of the epithelia, as when cancers of the liver contain bile, and those of the breast colostrum. Much that is called colostrum, however, is but masses of fatty degenerated epithelia derived from the duct wall. Traced back to the acini there is no relation between these and the "colostrum."

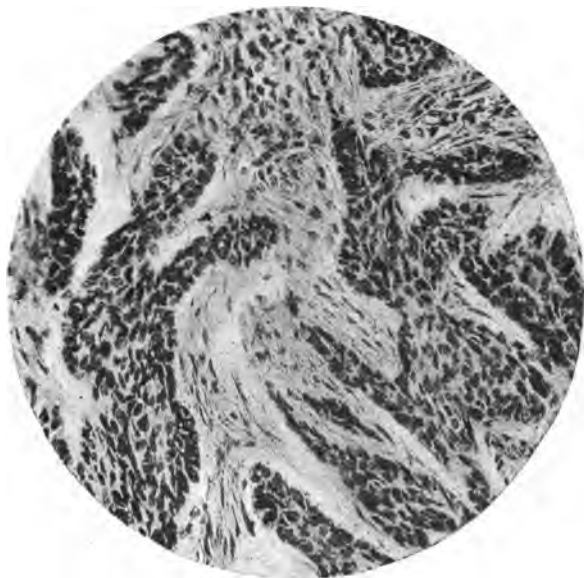
Fatty degeneration of a cancer resembles similar alterations elsewhere. The fat may occur in large meshwork and give the tumor a yellowish look and softer consistence; after resorption of the fat the tumor shrinks.

Mucoid degeneration may be like that observed in other tissues, or may be a solution of the cells in a viscid pseudo-mucin; hyaline and myxomatous degeneration may be observed in the same tumor; when well marked there are in the gross small grayish semitranslucent points or cyst-like cavities filled with sticky fluid. The highest grade of this degeneration, as often encountered in the carcinomas of the stomach and gut, has been considered a special variety and received the name gelatinous or colloid carcinoma. Often such a tumor has an alveolar structure which may be recognized by the unaided eye; because of the degeneration of the epithelium and reduced

energy of the neoplastic process, these tumors make but few metastases and grow slowly. Owing to disturbance of the tumor's nutrition liquefaction and other necroses may occur.

Rodent Ulcer.—On skin and mucous surfaces carcinomata almost invariably ulcerate and discharge thin, foul-smelling fluid; the edge of such an ulcer is usually thickened by the advancing epithelial growth, and looks like a sharply cut wall on

FIG. 39.



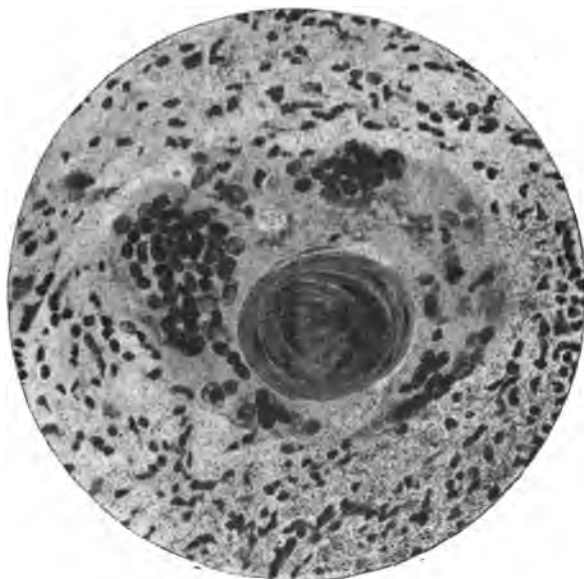
RODENT ULCER. (PHOTO.)

the ulcer side and slopes gently away on the sound side. A rodent ulcer and an epithelioma which is ulcerating may resemble each other, but in the former there is no cornification of the epithelia (hyperkeratosis) and its growth is very slow. Moreover, it starts in the basal layer of the epithelium and its cells remain embryonic, while in contrast to this the cells of

epithelioma return to an embryonic state, but afterward may resume their tendency to make cornified scales, hence the pearls or whorls so common in the latter but never seen in rodent ulcer.

Beside the degenerations mentioned, local collections of horny epithelia occur in cancer of the skin and mucous surfaces (tongue, cervix uteri, etc.), as onion-like, laminated spheres lying deep in the epithelial processes as in a lumen, with other epithelial cells packed closely round them. Calcification and pigment are not common in carcinoma. Hemorrhages in the

FIG. 40.



EPITHELIOMA. (PHOTO.)

Large whorl of laminated corneous epithelia surrounded by non-corneous cells.

tumor occur when cell growth is very free or after vessels are eroded by ulceration. Cysts may form from such hemorrhages or from softening and degeneration. Combinations occur with other tumors and with gumma and tubercle tissue, but not often.

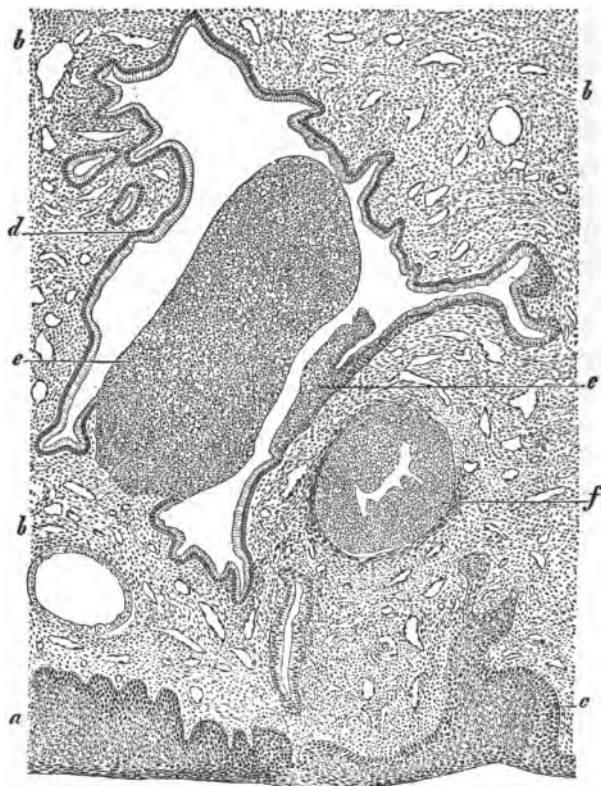
Carcinomata have been classified as scirrhus, encephaloid, colloid, etc., chiefly from their gross appearance, but a division according to the nature of the epithelial element and the type of gland represented is to be preferred. Thus we have flat-celled and cylindrical-celled carcinomas, adenocarcinoma and carcinoma glandulare solidum.

Flat-, Squamous- or Pavement-celled Carcinoma.—For this variety which is found where flat epithelia normally exist, as the skin and mucous surfaces, the name *epithelioma* is usually employed. It develops especially at lines of junction between skin and mucous membrane, as on the lip, the ala of the nose, the eyelid, glans penis, labia and portio vaginalis. It begins as an induration, usually not deep, circumscribed but vaguely; ulceration occurs early and may be rapid. The microscope shows large or small epithelia like those of the part which reach down into the tissue in straight or branching bundles, many of these exhibiting the whorls or pearls or cancrioid bodies of tightly packed horny cells. The term hyperkeratosis is used for the marked cornification of the epithelia, not only on the surface but deep in the intruding columns as well. This return to the type of corneous scales, as soon as the column stops growing, explains the formation of the characteristic pearls. These are laminated and tightly packed because of the pressure of surrounding tissues. Their presence is not essential to a diagnosis of epithelioma, for in a rapidly growing tumor proliferation may be so steady and continuous that there is no time, so to speak, to produce whorls.

Cylindrical celled epithelioma occurs especially in mucous membranes which have one or several layers of cylindric epithelium; the stomach, rectum, bile capillaries, cervix and corpus uteri are often involved; if cilia are normally present in the epithelia of the part the tumor cells may reproduce them but usually not. If it starts deeply in the mucous crypts of an organ it remains for a time as a broad infiltration, but soon it reaches the surface and presents an ulcerating appearance. Heterotopous

tumors of this kind may occur in the kidney, thyroid, bones and peritoneum. Microscopically the tumor is arranged in acini clothed with a layer of cylindrical cells, often two or more layers at some points, supported by varying amounts of stroma,

FIG. 41.



BEGINNING CARCINOMA OF PORTIO VAGINALIS. (Ziegler.)

a, superficial epithelium; *b*, fibrous stroma with vessels and lymph spaces; *c*, cone of epithelium invading the deeper tissues; *d*, mucous gland irregularly dilated; *e*, its epithelia proliferating in many layers and forming a large plug which protrudes into its lumen; *f*, gland cut across, showing less dilatation but the lumen nearly filled with atypical epithelia.

which may be degenerated ; later the cells may fill the acini to distention.

Carcinomata reproducing gland structure are called adeno-carcinomata and are common in the stomach, especially at the pylorus, the testis, ovary, uterus, breast, prostate and pancreas. They are described as occurring in the three forms of simple, medullary and scirrhus, according to the amount and proportion of epithelia and stroma ; practically the three forms are modifications of the same tumor. If simple, the proportion of stroma to cells is about as in most glands ; if medullary the cells are in excess and the tumor is soft ; if scirrhus the fibrous stroma is so developed that the tumor is very hard, and even under the microscope careful search is required to detect epithelial cells and thus its true nature, except in the younger portions. This form may be either nodular or diffuse ; on scraping a cut section with a knife a milky fluid is collected, made up of degenerated epithelia, and fat, in an albuminous fluid. The tendency to mucin formation is strong.

Paget's Disease.—Beginning as a quasi eczema of the nipple, the later stages of the disease are ulceration and a carcinomatous process, the epidermic cells showing inflammatory changes, vacuolation and edematous infiltration of nucleus and protoplasm. From its resemblance to other superficial malignant tumors it has been considered as a special form of flat-celled epithelioma. Because of the apparent presence of coccidia in the cells (vacuoles) it has been interpreted as a cancer in which the parasitic etiology is clear. The parasite is said to occur as small protoplasmic bodies which are at first free in the tissues, but then they enter epithelial nuclei, or protoplasm ; they develop further at the expense of the cell to sporozoa, and the nucleus divides and subdivides to form sporozoites, which are thin and slightly curved filaments. This parasitic explanation is not generally accepted.

Clinically the course of carcinoma is usually slow, requiring months or years before general symptoms occur ; but the rapid increase (from increased nutrition) in uterine cancer after the

establishment of pregnancy is an example of the effect of local causes in hastening the disease. When the growth and metastasis are rapid a profound cachexia develops which may be due

FIG. 42.



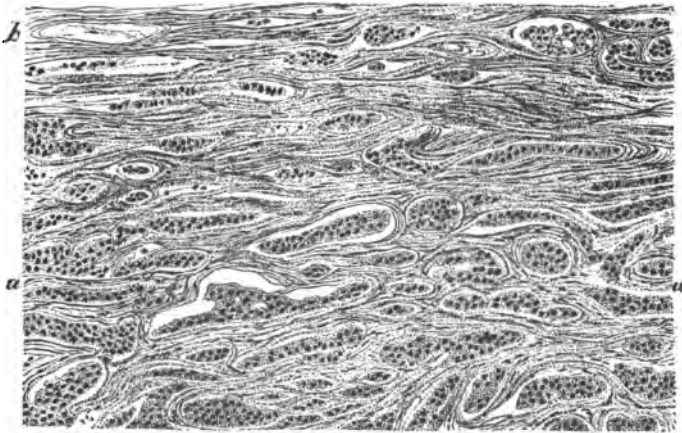
PAGET'S DISEASE. (PHOTO.)

either to the symptoms, as pain, the discharges from ulcerating points, the disturbance of glands by the formation of secondary tumors, or the absorption of some peculiar toxic substances from the misdirected function of the newly formed epithelia. The quantity of nutritive material of which the organism is robbed by the tumor is probably not a factor of importance in the cachexia.

The cause of carcinomatous formation is still a matter of uncertainty. Many influences of an irritative nature are noted, as in epithelioma of the under lip perhaps connected with the habit

of smoking, but the upper lip which seems as much exposed commonly escapes ; and age has an influence, for the majority of cancers occur after the fortieth year, when the tissue resistance throughout the body is beginning to diminish with the approach to senility ; and sex plays a part, for more women are the victims of cancer than men, although the occurrence of cancer on the skin and in the alimentary canal is more common among men : but no one of these nor all of them will explain why a carcinoma should develop. The idea of congenital inclusion of tissues is not so applicable to cancer as to sarcoma. Wounds of various kinds are usually a coincidence rather than a cause. The influence of heredity is no longer considered more than predis-

FIG. 43.



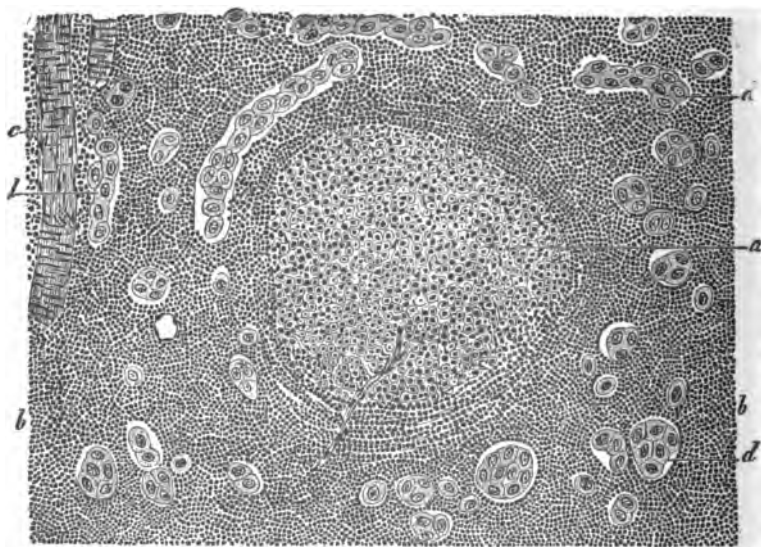
TUBULAR SCIRRHUS. (Ziegler.)

a, variously shaped columns of epithelia cut at different angles ; *b*, cells disappearing, stroma beginning to predominate.

posing. Analogies with certain conditions known to be due to parasites have occupied the mind of investigators for many years, and various forms of cell inclusion and degeneration have been regarded as the lower organism to whose entrance into the body the carcinoma is due. Transplantation experiments have suc-

ceeded in a very few cases and this apparent success has been taken as proof of the parasitic nature of carcinoma. But the spontaneous transplantation, by emboli, of a tumor situated elsewhere in the same body should not be forgotten, and the transplantation to another body may perhaps be explained as a piece of tissue rather than a germ finding conditions satisfactory for its growth. Fungi, bacteria, sporozoa, amebæ, gregarinæ, blastomycetes and coccidia have all been considered as the parasite, but none has been proved so far; form and staining properties

FIG. 44.



METASTATIC CARCINOMA IN LYMPH NODE. (Ziegler.)

a, mass of young cancer cells; *b*, lymphoid tissue of the node; *c*, small artery; *d*, fully developed atypical epithelia spreading along a lymph-vessel.

have been relied upon to demonstrate them, but cultivation and inoculation are required first before the matter can be decided. Granted that a parasite is demonstrated, the accessory and adjuvant influences, of which we know more at present, must still be considered in causation.

The whole course of the disease, however, does not correspond to any parasitic infection with which we are acquainted ; there are no sudden increases in the number of cases with periods of declining frequency, and the apparent steady growth in the prevalence of cancer is to be explained partly as improved diagnosis and partly as the indirect result of improved public sanitation, more people reaching the age when cancer develops in proportion as the length of a generation is extended. Granted for the moment that some parasites may cause tumors, as coccidia in the liver and Bilharzia in the bladder lymphatics, the view of malignant cell proliferation as accelerated "habit of work" refers parasites to the only importance which can be safely claimed, *i. e.*, one among many possible stimuli of such proliferation.

F. Cysts and Teratomata.

Under the name cyst many forms of tumor are grouped, consisting of a cavity lined with epithelium or not, containing more or less fluid material, serous, mucous, hemorrhagic, etc.; and also certain parasites occur in cyst form. The tumor is simple or divided into many smaller compartments, hence called multilocular, and the secondary cavities may be only in the wall of a large cyst ; by breaking down septa a multilocular cyst becomes simplified into one large cavity, the wall marked by incomplete partitions which persist. Many cysts remain stationary as small tumors, some grow slowly but steadily and may reach an enormous size, degenerations in wall and contents are common. Strictly speaking the exclusion from the economy of a blood extravasation or a degenerated area by the formation of a fibrous capsule is not an example of a cyst, nor similar formation about a parasite or foreign body. Apart from such forms we distinguish cysts developing in a body cavity and cysts of new formation.

Cysts of the first variety are usually called retention cysts and occur when a gland lumen or duct is closed and its contents accumulate, as from pressure, foreign bodies, stenosis and other

mechanical causes ; the contents may be that of the gland involved or the same variously altered. These cysts are further divided into follicular, mucous, and those of large canals. An example of the first is found in comedo, sebaceous cysts (sebato-ma) and of the Graafian follicle ; examples of the second occur often as polypoid growths on mucous membranes ; the third variety is observed in connection with large glands like the breast, the liver and the kidney. A special variety may be made of cysts developing in canals which normally disappear in the complete development of the body, as in the urachus, the parovarium, the hydatids of Morgagni, and the primitive branchial clefts.

Cysts of similar formation may be congenital and are divided into dermoid cysts and teratomata. They depend upon disturbances of development and dislocations of part of one or more embryonic layers. The dermoid cysts received their name from the resemblance between their walls and the normal skin, and in simplest form they contain epithelial scales and the products of their degeneration, hair, sebaceous glands and fat ; or they may also contain teeth, imperfectly formed bone and mucous tissue. They occur in the subcutaneous tissue, connected with periosteum, in the orbit and the antrum.

Teratoma is the name applied to such tumors when they contain portions of a more or less imperfectly developed embryo, like a limb or a gland, and they are found especially often about either end of the main axis, connected with the pelvis or the head. Where the inclusion approaches in completion the child at term, the case is referred to the double monsters.

Cysts of new formation, proliferation cysts, belong to the true neoplasms. They increase by formation of new tissue, accumulation of their mucin or colloid contents, and the degeneration and distention of new portions. They occur most often in the ovary, kidney, and testis, and are described as either glandular or papillary. (See Diseases of the Ovary, Pt. II.)

CHAPTER VIII.

ANIMAL PARASITES.

A PARASITE is an organism which lives in or upon another, and the most important are those which live at the expense of others. All degrees of parasitism are found, from simple coexistence and a common source of food (commensalism), to actual destruction of the host by the parasite. The subject has many sides, but from their disease-producing action certain kinds of vegetable and animal parasites require special mention; the vegetable comprise the fungi and the bacteria, and will be treated in Chapter IX.

The animal forms, for which the name parasite is reserved by common habit of speech, occur both on the surface of the body and internally; some go through only a stage of their life history as parasites, some are wholly parasitic, others are optional parasites, able to live apart from man (as certain mosquitoes which live on vegetable juices in the absence of animals). As nutriment is obtained without much labor, the organs of a parasite may be variously aborted, the external kinds retaining locomotive or grasping organs, the internal at times having no digestive or respiratory systems, since they absorb both gas and nutriment from the tissue juices; hence they may retain only reproductive organs and if the sexes are separate one may be more rudimentary than the other. Their reproductive energy in some cases is enormous.

The effects of parasites may be either mechanical or chemical. Mechanical are: Stoppage of lumen of gut, vessel or gland ducts; pressure; bleeding from direct suction, perforation of vessels after inflammation. As chemical may be mentioned:

Poisoning the host, irritation and inflammation, local necrosis, and many reflex nervous symptoms.

FIG. 45.



AMEBA COLI. (Stengel.)

Protozoa.

Rhizopoda. 1. *Amoeba coli*.—Occurs in intestinal contents, ulcers of gut, secondary abscess. Single spherical cell in quiet stages, puts out pseudopods when active, 15–25 μ in diameter, periphery hyaline, protoplasm finely granular; may contain red cells and bacteria; encysted form smaller and may show nucleus; found in great numbers in stools of tropical dysentery. Perforate mucous membrane of gut, cause necrosis, inflammation and secondary abscess of liver. *Amoeba coli* is said by some to be innocent and *amoeba dysenteriae*, another form, the cause of injury cited.

Sporozoa. *Gregarina*; *Coccidia*.—Cell parasites, widely distributed, spheroid or with one diameter much longer than others, covered by firm cuticle, make countless spores when encysted, which reach cells and develop, then become free in gut and

gland ducts ; move but little or are very active ; perhaps the best known form is the coccidium oviforme of rodents, of which the spores are called psorospermia. Another kind said to occur in molluscum contagiosum. Miescher's "tubes" (Sarcosporidia) are another instance of parasitic sporozoa ; they occur in muscles and fascia of mouse, hog, elk and man (rarely) as falciform bodies, often calcified, strongly resembling trichinae.

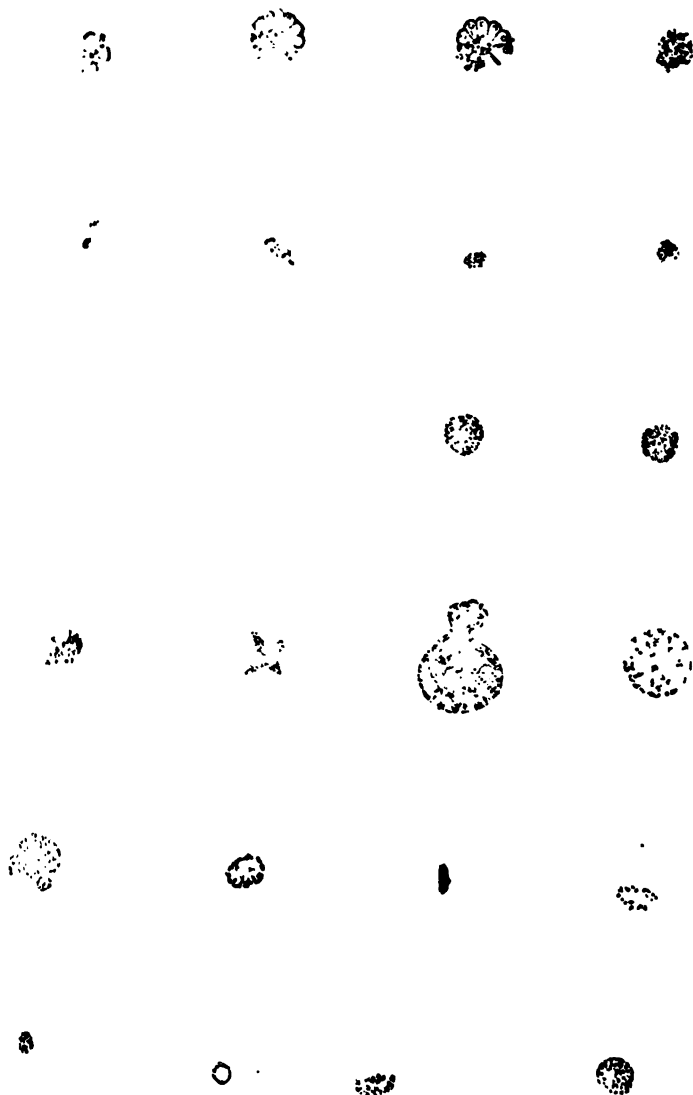
Acystosporidia.—Best known forms those of bilious typhoid, black-water fever, bird and human malaria and Texas fever of cattle (fam. Hemamebidae).

Malarial Plasmodium.—Parasite, one-celled, one stage of its life in mosquito (anopheles) and by it inoculated upon man. In the body of man occurs as ameba with active motion, or as long crescents usually motionless except pulsation ; both present hyaline protoplasm and a diffuse or distributed nucleus.

Ameboid form ; pale structureless disks in red blood cell ; inclose pigment granules as they increase in size, show ameboid movement till large adult fully pigmented stage is reached, while red cell changes in shape, size and color. Reproductive stage follows, the ameba quiet, pigment collects at center, rarely periphery (presegmenting form), delicate radii appear splitting ameba into segmenting forms (rosette) commonly 18 in number, disposed about a dark unsegmented residuum ; corpuscle breaks and sets segments free as small roundish or oval spores each with a central refracting nucleus ; these reënter red cells and repeat the cycle, which is thus equivalent to continuous self-inoculation of the host. Fever paroxysm and breaking up of rosette coincide. The second form of the organism which secures its existence outside of the human body (exogenous cycle) is produced by conjugation of a single flagellum of the "male" flagellate form with a large, pale non-ameboid "female." Three forms are recognized :

Tertian Parasite.—Life of each generation forty-eight hours, hence fever every second day ; with two broods maturing alternately fever becomes quotidian ; hence called double tertian by

FIG. 49.



ILLUSTRATING DIFFERENT FORMS OF THE MALARIAL ORGANISMS WITH THEIR STAGES OF DEVELOPMENT. (*From Tyson's "Practice of Medicine."*)

A_1, A_2, A_3, A_4 , sporulation stage; B_1, B_2 , sporules separating; C_1, C_2 , free sporules; D_1, D_2 , epi-corpuseular forms; E_1, E_2, E_3, E_4 , intra-corpuseular forms; F_1, F_2 , the large extra-corpuseular body; G_1, G_2 , the flagellate forms; $H_1, H_2, H_3, H_4, H_5, H_6$, the crescent-shaped parasite and its developmental changes in shape.

some authors. Adult pigmented form nearly or quite fills red cell, fifteen to twenty round or oval spores at a time set free from one red cell; this occurs in marrow and spleen or in peripheral circulation. Commonest type in temperate zone.

Quartan Parasite.—Broods mature every seventy-two hours, paroxysm of fever once in three days; with double or triple infection fever comes every two days with a free one following or every day. Ameboid stage refractile, clearly outlined, grows and moves slowly, no pseudopods found. Pigmented form contains few but larger granules, pigment darker, radiating lines more distinct, spores larger and fewer and nucleated, as are all malarial spores; red cell apt to be shrunk, not so decolorized. Segmentation in peripheral blood and internal organs.

Estivo-autumnal Parasite.—Fever caused are irregular, quotidian, tertian or pernicious, the latter remittent or continuous. Cycle varies from twenty-four to forty-eight hours. In smallest form the ameba seldom reaches size of red cell (about $\frac{1}{3}$) and cell may contain more than one. Young hyaline form is signet-ring-shaped with clear, non-staining center, may be found free in plasma; pigment absent or in small grains eccentrically placed; spores small, from six to thirty. Red cell shows no effect or shrinks, with coloring matter about the parasite and rest of cell paler. Crescentic form appears after paroxysm as round, oval or spindle-shaped bodies one-fourth the diameter of the red cell (young form of crescent); grow to be $1\frac{1}{2}$ diameters of red cell by one-fourth, and either spindles or crescents, homogeneous and highly refracting; pigment granules fine and grouped in mid zone; red cell may persist as delicate line like bowstring from end to end of crescent. Flagellate forms develop outside red cells, flagella appear suddenly and by their activity move the parasite or cause adjacent cells to move.

Outside the body of man exists in the stomach of anopheles as either hyaline or granular forms, the latter not flagellate; undergo changes in mosquito stomach for about 8-10 days and small

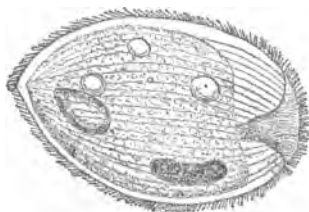
filiform bodies then found in poison glands of host ; from there introduced at time of stinging human body. See pp. 198-9.

CHIEF DIFFERENCES BETWEEN THE PARASITES.

TERTIAN.	QUARTAN.	ESTIVO-AUTUMNAL.
Cycle in man 48 hours,	3 days,	24-48 hours.
Ameba in red cell active,	sluggish,	smaller than tertian.
Decolorizes red cell slowly,		hemoglobin deeper in tint.
Causes red cell to swell,	size preserved or diminished,	red cells shrivel.
Outlines not sharply defined,	sharp,	
Pigment in fine granules abundant, in motion,	coarser, fewer,	pigment in fine peripheral granules, not often in motion.
Spores 15-20, usually 18, small,	6-12, larger,	small, 6-30, usually 18.
Flagella more numerous,		less numerous.
Ring forms common, early, more distinct than those of estivo-autumnal,		common, ring and disk forms less distinct.

Infusoria.—Bodily structure more complicated, consisting of ectosarc, sometimes striate, and endosarc, granular ; present rudimentary intestinal canal with differentiated openings which lead directly into the protoplasm ; may have a pulsating vacuole which is both circulatory and excretory in function ; surface covered with cilia ; reproduction by fission or conjunction of two. Divided into flagellata, ciliata and suctoria.

FIG. 47.



PARAMECIUM COLI. (*Delafield and Prudden.*)

Ciliata.—Most important are *cercomonas intestinalis*, pear-shaped, transparent, $8-10\ \mu$ in length, with short blunt tail and long delicate cilium which thrashes in medium and produces locomotion; found in feces of diarrhea, cholera and typhoid; *trichomonas vaginalis*, oval, $15-25\ \mu$ long, single cilium at one end and bundle of cilia at other, undulating membrane on the side; found in urine, vaginal secretion and sputum; and lastly, *paramecium coli*, ovoid, .06-.1 mm. long, one or two contractile vacuoles, surface covered with cilia; found in diarrheal feces and sputa from abscess of lung.

Vermes.—Animals in segments usually, with laterally symmetrical cylindric or flattened bodies, without appendages except bristles or clinging apparatus; internal organs complicated, at times blood, nervous and digestive systems present, or one or all may be lacking; sexes separate or coexist; most important parasites of men and other vertebrates. Chiefly occur as flat and as round worms:

Flat worms (Platyhelminths).—

Cestodes—Tapeworms:

Tenia solium and *mediocanellata*,
Echinococcus,
Tenia nana and *cucumerina*,
Bothriocephalus latus.

Trematodes—Sucking worms.—

Distomum hepaticum, *lanceolatum*, *hematobium*.

Round worms (Nemathelminths).—

Acanthocephali:

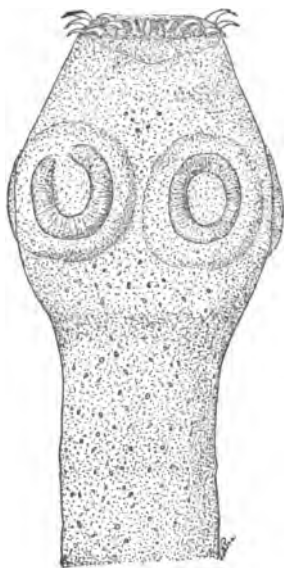
Echinorhyncus hominis.

Nematodes:

Ascaris lumbricoides, *mystax*,
Oxyuris vermicularis,
Eustrongylus, *Strongylus*, *Dochmius*,
Anguillula stercoralis,
Trichocephalus dispar, *Trichina spiralis*,
Filaria medinensis, *Filaria sanguinis hominis*.

The flat worms have either segmented (Cestodes) or unsegmented (Trematodes) bodies, flat and tongue- or leaf-shape, a branched excretory system, intestine absent in Cestodes, present in Trematodes, external prehension apparatus as hooks, sucking disks, etc., hermaphrodite.

FIG. 48.

HEAD OF TENIA SOLIUM. (*Delafeld and Prudden.*)

Cestodes, Tapeworms.—Without mouth or gut, consist of a head (scolex) and segments (proglottides), the latter rectangular and increasing in size with the distance from the head, the largest end segments breaking off and passing out of the host in the feces; eggs are produced in the larger segments. On plants, in water or manure, remain for a time and then swallowed with the food of another animal, the egg coverings digested off and embryos set free; they bore into the tissues or vessels of the host and develop in various organs to bladder-like larvæ, from whose walls new sexless individuals form; these passively gain

entrance to a new host (through use of animal food) and develop to a new colony of segments.

Tenia solium.—Frequent in man, several meters long, coiled in the gut or stretched, may be several present, head 1 mm., segments 10 mm. by 6 mm., head furnished with a rostellum and 26 hooklets, behind which are four sucking disks, eggs ovoid, about 35 μ long, embryo occurs as measles in pork and as cysticercus cellulosæ in muscles, brain and eye of man. Occurs specially in cooks, butchers and those who eat imperfectly cooked pig meat. The worm develops quickly in the lower part of the small intestine, may reach a length of 2-3 meters in as many months, and may persist 10 years.

Tenia mediocanellata (saginata).—May be 6 meters long, head 2.5 mm. broad, no hooks or rostellum, four strong disks usually surrounded with line of pigment, segmentation in the neck evident to the naked eye, uterus has many side branches which divide dichotomously; grows as a whole about 12 segments a day; eggs more oval than *T. solium*, with a thick shell and lining membrane; proglottides passed singly; common, usually single, follows use of uncooked infected beef.

Tenia echinococcus.—Occurs in domestic animals as a small, trisegmented worm, about 4-5 mm. long, rostellum conical, 28-46 hooklets in two rows; last segment has a branched uterus, irregular, full of long oval eggs. Larvæ gain entrance to human intestine, wander into various tissues, especially the liver, and slowly develop into cysts with a wall in many layers; after five months the daughter cysts develop from the inner wall of this, projecting into the fluid contents of the main cysts (*echinococcus hominis*, *endogena*) or more rarely project outwardly (*e. scolicipariens*, *exogena*). Cyst contents clear, free from albumin; may reach an enormous size, may degenerate by absorption of fluid and fatty changes. From the dog as only known source. Clinical importance of such cysts according to size and location; found in liver, lung, peritoneum, skin, muscles, kidney, spleen and brain. Most common in Iceland.

Bothriocephalus latus.—Largest human tapeworm, may be 8 meters long (3-4 thousand segments), head looks like a swelling of the thin neck, marked by two deep sucking furrows arranged longitudinally, segments 10-12 mm. broad by 5-8 mm. long, passed in groups; uterus a simple canal variously bent from side to side in the middle of a ripe segment; eggs oval, brownish, develop in fresh water to a ciliated, freely moving sphere; occur in certain fish (as the pike) and especially in Switzerland, and by their use as food in human beings also.

Trematodes, Sucking Worms.—These parasites as found in human beings are members of the family Distomidæ, internal parasites with a sucking organ at the oral aperture and another on the abdominal aspect, the intestine is forked and ends blindly, the uterus contains oval eggs which even in the parent develop into ciliated embryos; divided into two groups, the distoma with hinder sucker in the cephalic half, and amphistoma with the second sucker at the posterior extremity.

Distomum hepaticum.—Shaped like a flat high-shouldered bottle, 15-40 mm. long by 12 broad, tapers more sharply backward, both suckers small and near together at the head end, between them the genital pore; hermaphrodite, the pore serving as common duct for both sets of organs, often presents a thick spiral cirrus (penis), multiplies by junction of two, each acting as both male and female; eggs oval, 0.13 mm. long. Worm occurs in liver, in gall-ducts and bladder, usually few at a time in man, causing inflammation of gall-passages; may penetrate vessels and be carried elsewhere.

Distomum hematobium.—Body longer, flat in male, more cylindrical in female, suckers at head end and close together, color white; male 12-14 mm. long, female 16-19 mm., eggs 0.12 mm. long, oval and somewhat pointed at poles; occurs in ureters, bladder and colon and causes inflammation (dysentery, pyelitis), found in Egypt specially. Embryos develop in water and may have a mosquito or a crustacean as temporary host.

Round worms (Nemathelminthes), of small or large cylin-

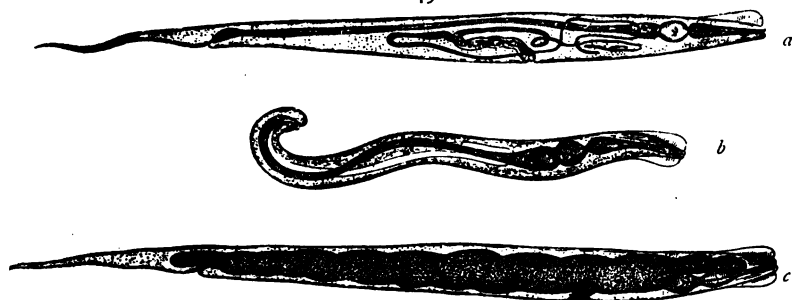
drical form, ringed but not segmented, sometimes with hooks or papillæ at the anterior end, blood and breathing organs absent, sexes separate.

Acanthocephali.—Only member of this order is the *Echinorhynchus hominis*, 5–6 meters long, with 12 cross rows of hooks, 8 in each row; very uncommon.

Nematodes.

Ascaris lumbricoides.—Commonest intestinal parasite in man, cylindrical body tapering toward each end, four longitudinal stripes and many cross ones; male 250 mm. long by 3 mm. thick, female 400 mm. long by 5.5 mm. thick, color pale red, head slightly different in color, intestinal canal runs through the entire worm to a vent on the hinder abdominal surface; tail end of the female somewhat blunt, double uterus, thread-like and twisted, may contain as many as sixty million eggs; these are oval, with a thick shell, about 0.05 mm. long, covered by a layer of albuminous matter which preserves them for a long time after extrusion; may be no intermediate host, the eggs swallowed and immediately developed in human intestine; may be single or in countless numbers; produce catarrhal inflammation of the gut, obscure nervous symptoms, perforation and abscess, or stoppage of various lumina, as gall-ducts.

FIG. 49.



OXYURIS VERMICULARIS. (Birch-Hirschfeld.)

a, mature unfertilized female; *b*, male; *c*, female after impregnation, the enlarged ovary concealing other organs.

Oxyuris vermicularis; *Thread worm*, *Seat worm*.—Small white thread-like worms, male about 3–4 mm. long, female 8–12 mm. long, tail of former rolled up, tail of latter very tapering, mouth end provided with three lips in each; genital pore posterior in male, anterior in female; intestinal canal straight and in the mid-line; eggs oval, 0.05 mm. long and contain an embryo with sharp posterior end. One of the common human parasites, in adults as well as children, chiefly in colon and about rectum and anus, from here may enter the vagina; produces catarrhal inflammation, nervous symptoms, great itching about anus; may be transmitted from use of common privies or the eggs may be dried and gain entrance by swallowing.

Eustrongylus gigas, *Palisade Worm*.—Uncommon, found in the renal pelvis at times, female 1 meter long by 8–12 mm. thick, male 0.5 meter, red color, male has bell-shaped copulatory bursa posteriorly, six papillæ about mouth, no pharyngeal dilatation.

Strongylus.—A small worm of this group has been found occasionally in the lung or the duodenum; gray white in color, mouth small with two papillæ on neck, bursa shallow, cupped.

Dochmius.—Mouth wide, furnished with teeth, lips hard, two claw-shaped hooks on ventral side of mouth, two smaller ones on dorsal edge.

Dochmius duodenalis, *Anchylostomum duodenale*.—Male 10 mm. long by 1 mm. thick, female 12–18 mm. long, body cylindrical, head bends toward dorsal aspect and furnished with a horny mouth capsule with two teeth ventral and one dorsal, gut large and often blood-filled, hind end of female pointed, of male arranged as a three-leaved cup; eggs oval with thin shell, about 0.04 mm. long; parasitic in upper part of small intestine where it clings to the mucous membrane and sucks blood for its nourishment, often in numbers; on separation from gut wall a small ecchymosis is left with a pin-point bleeding hole in the middle: if present in great numbers may cause a serious anemia, which may be fatal or lead to other disease. Occurs especially in Egypt and Brazil.

Anguillula stercoralis.—Uncommon except in China, occurs in gut as extremely fine thread, 0.25 meter long, causes diarrhea, dysentery, anemia and emaciation.

FIG. 50.



TRICHOCEPHALUS DISPAR. (Birch Hirschfeld.)

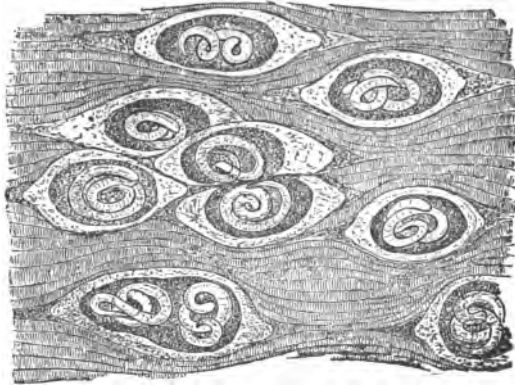
Natural size. *a*, female; *b*, male.

Trichocephalus dispar.—About 4 cm. long, anterior end long and very thin, small mouth without papillæ, occurs singly or in numbers in cecum and ascending colon, may pierce the gut wall if continuity broken by ulceration, otherwise appears to cause but little trouble.

Trichina spiralis.—In two forms in man and animals, as developed worms in the intestine, and as encapsulated in the muscular tissues; among animals most common in hogs, found also in rat, fox, bear, cat, and other carnivorous or omnivorous animals. Intestinal form thread-like with thinner head end and round tail end, male 1.5 mm. long, female 2–4 mm. long; intestinal canal divided into pharynx, stomach, gut, and ends in a cloaca with the genital apparatus; eggs 20 μ in diameter, pierced by embryo while still in uterus and brought forth alive after 5–7 days in the stomach, this process may last several days with a total of 1,500–2,000 young worms, which bore through the walls of the alimentary canal and find their way to the voluntary muscles, the exact road travelled being still a matter of dispute, either passively by the blood stream, or actively by way of the connective tissues and lymph channels; probably passive manner far more important; after the brood is hatched the female dies and is passed in the feces; the male usually has disappeared

earlier. As early as two weeks after infection the worm may be found in the striated muscle within the fibers, where granular degeneration of the contractile substance occurs; then the worm rolls into a coil and lies in a lemon-shaped capsule which gradu-

FIG. 51.



TRICHINA SPIRALIS. (Ziegler.)

ally becomes infiltrated with lime salts (6-18 months), showing as a small white point to the naked eye. Thus encapsuled the worm may remain as long as 18 years capable of development as soon as it reaches a stomach whose gastric juice can dissolve the capsule and free it; but they may also die and be absorbed; after the death of the host the worm withstands the process of decomposition for weeks. Occurrence in man depends greatly upon methods of preparing meat (pig) for the table; where properly cooked the danger of infection is small as a temperature of 65°C., at which point the meat changes from a red to a gray color, destroys the worms; long pickling and smoking destroy the worms in the superficial parts of the meat but the central parts may still contain live ones.

Filaria medinensis, Guinea Worm.—Female 1 meter long by 2 mm. thick, circular oral aperture with four hooklets, tail pointed;

uterus fills the greater part of the body and contains countless embryos with pointed tails ; occurs in the tropics in the subcutaneous tissues, especially of feet and legs, causing bleeding and inflammation ; embryos live free in fresh water and occur in crustacea as intermediate host.

FIG. 52.



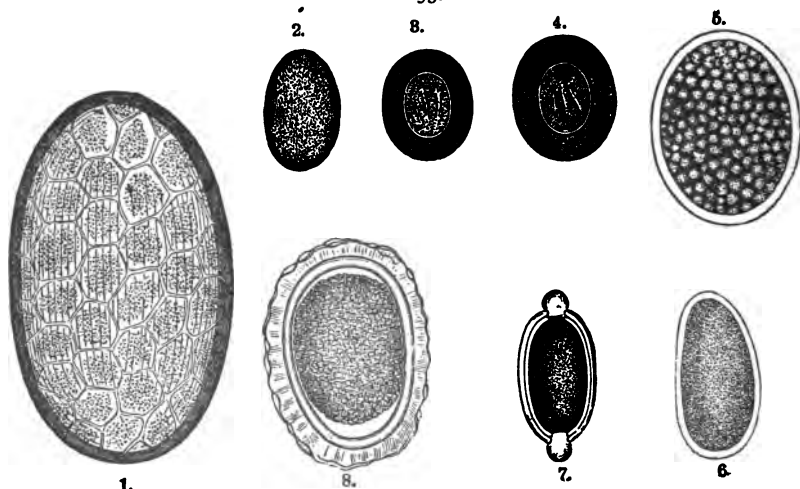
INTESTINAL FORM OF TRICHINA WITH EMBRYOS. (*Birch Hirschfeld.*)

Only the middle portion of the worm shown.

Filaria sanguinis hominis.—Embryos occur in the blood of patients in tropical countries causing hematuria and chyluria, 0.35–1 mm. long by 0.006 mm. broad, head blunt, tail tapering, one drop of blood may contain 6–12, appearing periodically (as at night alone), extruded from the kidney where they cause bleeding and loss of lymph. The developed worm occurs in the subcutaneous tissues and causes lymphangitic elephantiasis, as of scrotum and legs. Common in Egypt, India and China ; intermediate host probably a mosquito, set free in water by the death of the same and so carried to man.

Arachnoidea ; Insecta.—External parasites are chiefly members of the spiders or insects which cause inflammation of the integument by boring and biting, and are usually only an inconvenience. Most important for man are such forms as act the part of intermediate host for some internal parasite and particularly the fly, which mechanically carries typhoid bacilli from feces to the food of man and so spreads the disease, and the mosquito, which in some of its forms carries *filaria sanguinis hominis*, the bacillus of tetanus, the plasmodium of malaria and the unknown agent which produces yellow fever. The plague is propagated indirectly by ants, mice and rats, as typhoid by flies.

FIG. 53.



EGGS OF VARIOUS INTESTINAL WORMS. (Birch Hirschfeld.)

1, *distomum hepaticum*; 2, *distomum lanceolatum*; 3, *tenia solium*; 4, *tenia mediocanellata*; 5, *bothriocephalus latus*; 6, *oxyuris vermicularis*; 7, *trichocephalus dispar*; 8, *ascaris lumbricoides*.

The malaria-carrying mosquito is proved to be one of the genus *Anopheles* (especially *A. quadrimaculatus* or *claviger* and *A. punctipennis*, though probably others also). Texas fever, bovine malaria, is carried by a tick (*boophilus bovis*); a similar

disease of birds by *Culex pipiens*. In non-malarial countries only *Culex* occurs, in malarial the genus *Anopheles* also. This genus is described as follows : Palpi in both sexes about as long as the proboscis, 4-jointed in female, 3-jointed in male, though a constricted basal joint seems to add another to each ; palpi straight filaments and in female held parallel with proboscis except when biting, then raised and divergent ; nucha has posterior scaly cornu, abdomen pilose on both surfaces, not scaly ; legs long and end in simple unguis or dentate claws ; wings often spotted and magnifying glass shows spots made up of black squamæ on brownish wing ; length, including proboscis, female 7.5-9 mm., male smaller and does not sting ; resting on perpendicular surface, as a wall, *Anopheles* stands with main axis at right angles except when heavy with blood, *Culex* holds body parallel.

Cycle within mosquito—a flagellum (or microgamete) of the flagellate organism unites with ameboid (macrogamete), the former the “ male,” the latter the “ female ” ; then the fertilized ameba develops between the muscle fibers of the mosquito’s mid-intestine, takes on capsule and becomes sporozoon ; its nucleus divides and subdivides to form sporozoites, very slender filaments with curved ends and in middle a nucleus, with a little chromatin in rods and bundles ; the capsule breaks, sporozoites distribute through body and gather especially in salivary gland, thence inoculated at time of stinging : the cycle takes 8 to 10 days. As the form in the mosquito is more highly organized than the forms in man, he is the intermediate host for the insect’s parasite.

Culex fasciatus, the mosquito which carries yellow fever, has not been completely studied and the parasite has not been identified, so that its cycle of development may not be given ; but the mosquito having bitten a person suffering from yellow fever may after a period of about 12 days give the disease to one who is not immune ; blood taken from a case of yellow fever during the first or second day will give the disease when injected into the circulation of a non-immune ; an attack from the bite of the mosquito makes one immune against such injection. This

is all that may be asserted as yet. This mosquito has lately been taken from the genus *Culex* and with some others classed in a new genus, as *Stegomyia fasciata*.

Other external parasites, as itch insects, ticks, lice, etc., cause skin lesions which may be studied in any standard work on dermatology.

CHAPTER IX.

VEGETABLE PARASITES.

UNDER the head of microorganisms are grouped :

Saccharomycetes or Yeast fungi,
Hyphomycetes or Mould fungi,
Schizomycetes or Fission fungi.

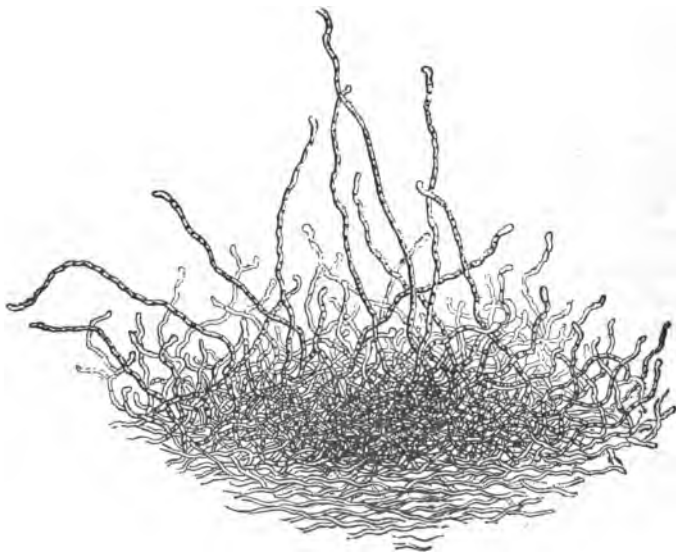
These all belong to the lowest plants, the non-chlorophyll-forming thallophytes, and are parasitic both upon and within the body of man, animals and other plants, but so far as man is concerned the latter (schizomycetes) are by far the most important because of their frequent causation of disease and consequent relation to hygiene and preventive medicine. They all derive their nutriment from more complex compounds of carbon, and if from dead organic substances they are called saprophytes, if from living tissues, parasites ; both occur in man.

Yeast fungi occur as harmless saprophytes in man, naked or encapsuled cells of round or oval form, and are constant in the alimentary canal, especially in the mouth and stomach ; if found in the bladder which contains urine and dextrose fermentation may occur with gas formation. Certain species may occasion suppurative inflammation of the various tissues but very rarely. The cells multiply by budding and the bud after reaching a certain size is constricted off ; when nutritive material is scant they may form sterile threads.

Mould fungi play an important part in certain superficial disorders of skin and mucous membranes. They occur as threads (hyphæ) woven together into a tangle (mycelium) from which certain filaments rise bearing short cylindrical or round cells,

the spores, grouped or singly. Though growing on the skin, in the hair, on the mucous membrane of mouth and vagina, they do not live on cells of good vitality but on those dying or dead ; less often they appear in more central parts, for the temperature is too high and the oxygen supply too low. A common form is the fungus of thrush, or aphthæ (*Oïdium albicans*) which may occur in the normal mouth without symptoms but in the debilitated may grow at the expense of the tissues.

FIG. 54.

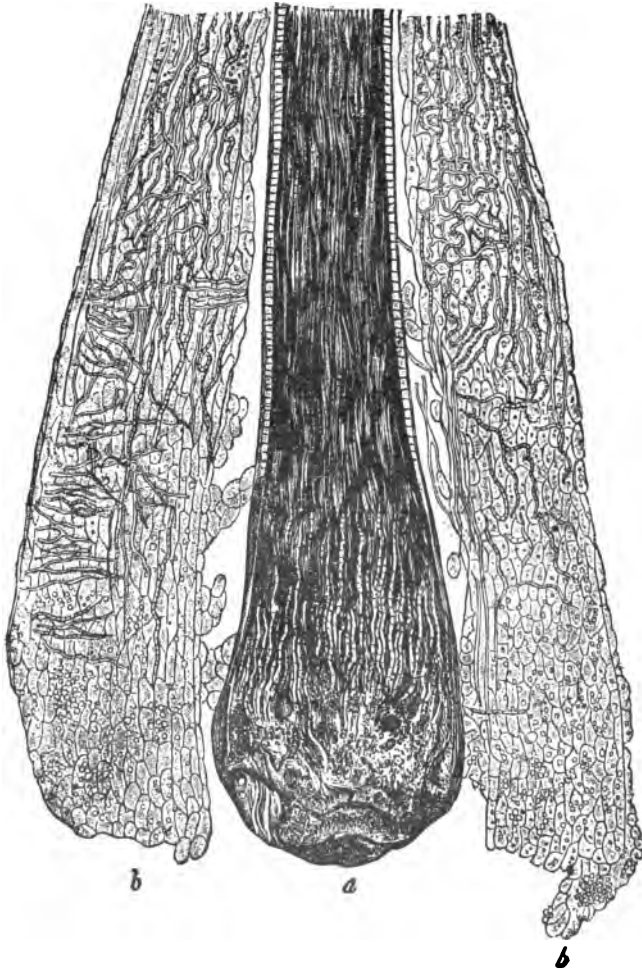


OÏDIUM ALBICANS ON THRUSH FUNGUS. (*Birch Hirschfeld.*)
Growth from mucous membrane.

Thread fungi produce various skin diseases, as favus, pityriasis versicolor, herpes tonsurans, etc.

Microsporon furfur, fungus of pityriasis versicolor ; delicate threads in the outer layer of the skin of the breast and back, causing peculiar branny and brownish spots from simple points to several centimeters wide ; in scrapings a mycelium of thin

FIG. 55.



HAIR WITH FAVUS. (*Kaposi.*)

a, hair infiltrated by mycelial threads showing few spores; *b*, its sheath, showing many spores.

branching threads, 1-2 μ broad, empty or filled with spores ; between the threads lie spherical groups of spores.

Microsporon minutissimum occurs occasionally in the skin in parts usually covered, causing brownish patches but little scaly ; resembles *M. furfur*, but is more delicate.

Trichophyton tonsurans occurs on hairy parts (scalp) affected with herpes tonsurans, causing partly bald, round spots of grayish color and covered with moist or dusty material, presenting broken hairs here and there ; the dust is made of dried epithelia and fungus spores which are more numerous than the mycelium and fill the hairs from root to outer end, 0.004-0.01 mm. in diameter, often arranged in chains ; free ends of hyphæ rounded. In *sycosis parasitica* and *eczema marginatum* a fungus is found which is said to be identical with that of herpes tonsurans, as also perhaps with that of ringworm.

Achorion Schoenleinii.—This fungus, the cause of favus, is found as continuous or segmented hyphæ with branches at right angles, homogeneous or granular, ends somewhat pointed, mycelium more numerous than spores, which are long oval in shape, 0.005-0.008 mm. in diameter : develops in the hair-follicles, surrounds the bulb and pierces the hair, growing throughout its different layers ; in the gross there are round, yellowish plates each about 10 mm. broad, pierced by a broken hair, easily lifted from its bed and hiding below it a drop of thick yellow fluid, these join and make large thick crusts of an unpleasant mouse-like odor. This fungus is passed from one patient to another readily and may invade hairless parts, as the nails and even the lung and intestine.

In general the fungi are more frequently pathogenic for lower animals than for man.

Schizomycetes : Fission Fungi.

Three chief morphological groups of bacteria are usually given :

1. Coccus or spherical, single or in groups ; if two occur together, diplococcus ; if four, tetracoccus, meris-

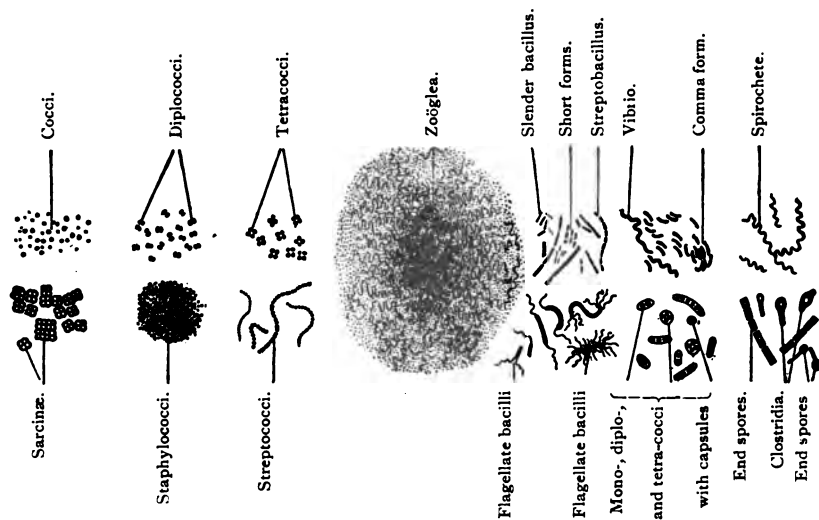


- mopedia ; if eight or more, sarcina ; if in chains, streptococcus ; if in bunches like grapes, staphylococcus ; irregular masses, zoöglea.
2. Bacillus, rod-shaped ; in twos, diplobacillus ; in chains, streptobacillus ; certain long forms are called leptothrix ; spindle shapes, clostridium.
 3. Spirillum, comprising the vibrio, short, bent like a comma, with a single leuc-flagellum, sometimes arranged in series ; the true spirillum, long, spirally twisted and rigid, usually with polar flagella ; and the spirochete, long, slender, spiral, pliant, without flagella.
 4. Pleomorphic forms :
 - (a) Cocci and short rods which develop to long threads forming arthrospores (proteus).
 - (b) Filiform bacteria with distinction between the ends, non-branching (leptothrix).
 - (c) Filiform with ends differentiated, branching (cladotrix).

Biology of Microorganisms.—Bacteria or germs are composed of plasma (mycoprotein) enclosed in a membrane ; in addition some forms have a capsule. Cocci are non-motile, in the other groups many kinds move actively, owing to the possession of flagella, thread-like processes capable of thrashing movement, some having but one, others many. Multiplication occurs by transverse division and is very rapid in good nutritive media ; when the supply of nutriment is beginning to fail and sometimes otherwise, many bacteria show a second manner of propagation, by spores, which are formed inside the sheath of the germ (endospores), either in the middle or at one or both ends, or separated off from the end (arthrospores). Multiplying by fission, if they remain in linear series and attached they form streptococci and streptobacilli ; if irregularly heaped together the condition is expressed by staphylo- and is found only in the cocci ; massed

and surrounded by a mucilaginous common envelope the term zoöglea is applicable. With the loss of nutrition various distorted involution forms occur.

FIG. 56.



THE FORMS OF BACTERIA. (Coplin.) Magnified 700 times.

Chief Forms and Sources of Nutriment.—Preformed organic matter soluble in water, water itself in plenty, potassium, sulphur, calcium, magnesium, etc. Carbon may be obtained by bacteria from soluble carbohydrates, weak alcohol, carbolic acid and other chemicals which in strong solution would destroy them; nitrogen from albumins, amines, amides, nitrates and ammonia; sulphur from various salts of sulphuric acid. The relation to oxygen is important :

Microorganisms requiring oxygen are called *aërobic* ;

“ able to grow in it, *facultative* “ ;

“ unable to grow in it, *anaërobic* ;

“ able to grow without it, *facultative anaërobic*.

Carbon dioxide restrains the growth of some germs (proteus) but is without influence on others (typhoid bacillus).

Sunlight by its blue, violet and actinic rays will destroy even the most virulent in the presence of oxygen, owing to the formation of H_2O_2 .

Temperature is of the greatest importance, each variety having its point of best growth (temperature optimum) and exhibiting less activity as the heat varies from this; but even in the cold produced by liquid air many forms are not destroyed, growth reappearing when the temperature is raised; and at higher ranges of heat than the optimum a culture may merely lose some of its vigor. The highest point reached is about $65-70^{\circ} C.$, at which level the bac. thermophilus will flourish, but as a rule $50-60^{\circ} C.$ gradually weakens and then destroys almost every form; the spores show more resistance to heat, as to other influences, for while boiling water and steam at $100^{\circ} C.$ will kill all bacteria, certain spores will endure this extreme for a time, and in the absence of moisture a temperature of $140^{\circ} C.$ may be necessary to kill them. Temperature optimum and pathogenic powers for man stand in close relation, those bacteria which cause disease being varieties which grow between $10^{\circ} C.$ and $45^{\circ} C.$, with optimum about 37° , the body temperature Grouped according to temperature :

Bacteria growing between	$0^{\circ} C.$	and	$30^{\circ} C.$	are	psychrophile,
"	"	"	10	"	45 " mesophile,
"	"	"	40	"	70 " thermophile.

Drying stops multiplication and then destroys most bacteria, sometimes being preceded by spore formation and the spores persisting indefinitely. Many chemical substances, including the products of the bacteria themselves, restrain or destroy them; as used in medicine such chemicals are called antiseptics and for most purposes are sufficient if they only prevent multiplication and active growth. Of these chlorine, bromine, carbolic acid, potassium permanganate, mercuric chloride, and formaldehyde are the commonest.

(See table of antiseptics, p. 314.)

Different kinds of bacteria in the same medium may assist each other's growth (symbiosis) or overwhelm each other.

Certain bacteria form various pigments (bac. prodigiosus and pyocyanus), others are phosphorescent, others form acids or cause various fermentations, and these special properties depend closely upon the conditions of best growth, being lost for a time when nutrition, etc., fail; but of all bacterial products those poisonous to human tissues are most important here. By their activity in splitting higher chemical compounds into more simple, bacteria form several kinds of products, as:

- A. Proteins: called pyogenic if causing suppuration, pyrogenic causing fever, phlogogenic causing inflammation. The protein of glanders (mallein) and of tuberculosis when injected into man or animal suffering from these diseases will cause a marked rise of temperature; used chiefly for diagnosis in veterinary practice.
- B. Ferments: these are assumed to exist from certain effects which they explain, act apart from the bacteria producing them (as in filtered cultures) and resist antiseptics; splitting up carbohydrates is called fermentation, similar action on albumins is called putrefaction, the ferments, enzymes.

Chief ferments: acting on

Proteids, dissolving them in alkaline medium, like trypsin;

Milk, coagulating it and dissolving the curd, like pepsin;

Fat, forming glycerin and fatty acids, like steapsin;

Sugar, inverting it;

Starch, forming sugar, like ptyalin;

Urea, forming ammonium carbonate.

- C. Other products of great variety, as
 - 1. Acids; acetic, butyric, formic, lactic;
 - 2. Aromatic substances; indol, phenol, skatol;

3. Derivatives of proteid digestion, albumose, peptone ;
4. Gases, CO_2 , H_2S , PH_3 , NH_3 ;
5. Nitrogen compounds ; amins, leucin, tyrosin ;
6. Ptomains ;
7. Toxins.

Ptomains and Toxins.—A ptomain is a basic substance, contains nitrogen, is found in putrefaction of proteid matter, and resembles alkaloids in its action, combining with acids to form salts ; at one time considered the essential element in bacterial intoxication. Toxins are formed by most all pathogenic bacteria, both by analysis and synthesis, in the living organism ; do not act like basic bodies, cause symptoms like animal and plant alkaloids (snake venom, abrin, strychnin), and vary with the source, each kind of bacteria having its own specific toxin ; their effect on the human organism is immense in minutest dosage, not only constitutionally but also locally to less degree. The power of the organism to resist is shown in the time of incubation necessary for the elaboration of sufficient poison after the entrance of the germs ; the percentage rises up to the limit of the emunctories to eliminate and the tissues to oxidize it, causing only indefinite symptoms of malaise, but just beyond this limit occur the symptoms of general poisoning, chills, fever, vomiting, etc. Toxins were thought to be albuminous in nature and called toxalbumins, but now they appear allied rather to peptones. They are destroyed by exposure to sunlight, heating at $60-80^\circ \text{C}$., and the gastric juice ; to cause symptoms they must appear in the blood ($1/275$ of a grain of tetanus toxin is fatal to an adult) ; they seem to have selective actions on certain cells.

Taxis.—Bacteria show three kinds of taxis, those to which they are susceptible and that which they cause ; thus

Phototaxis is exhibited by many forms, for they arrange themselves especially in the red and the blue rays when exposed to a spectrum.

Chemotaxis is the response to chemicals; positive, if the bacteria are attracted (aërobics by oxygen, typhoid by potato juice); negative, if repelled.

Cytotaxis is the power of the bacterium to attract certain cells; tubercle bacilli are negatively cytotoxic for pus cells (polymorphonuclear leucocytes), but positive for lymphoid cells.

Staining Reaction.—Many bacteria have special affinities for certain anilin stains and certain staining methods are of value in identifying them because of this relation; see Gram's method, p. 304.

Pathogenic Cocci.

Micrococcus (Staphylococcus) pyogenes aureus.—Found everywhere, especially in pus; spherical, $0.8\ \mu$ diameter, singly, pairs or groups, not motile, facultative anaërobe.

Culture.—Gelatine. In stick grows as fine white line along puncture, develops yellow to golden color by third day, liquefies the medium and falls as yellow precipitate.

Agar.—Opaque irregular white or yellow film, becomes more golden, clouds the agar, but does not liquefy. On plates, potato and serum grows freely. T., $30-37^{\circ}\text{C}$.

Pathology.—Injected into skin causes abscess; in the veins, multiple embolic abscesses, with fever, etc. (pyemia).

Stains with usual methods; G. +.¹

M. pyogenes albus is like the above, except in producing no pigment, forming a white film on media; m. pyog. citreus produces a lemon-yellow pigment.

Micrococcus pyogenes tenuis.—Found in certain suppurations, not motile, singly and grouped, $0.9-1.0\ \mu$ diameter, aërobic. Grows as small transparent circles or streaks, gelatine and agar. Causes no symptoms in animals; stains with usual dyes.

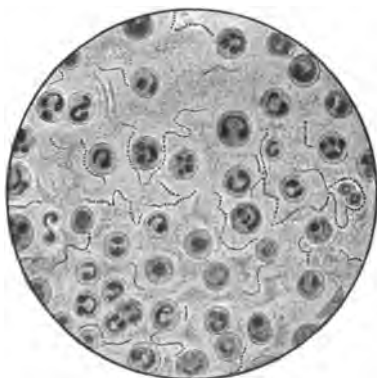
¹ In the descriptions of bacteria, plus and minus signs are used to denote behavior with Gram's method, G. + meaning that an organism stains with it, G. — that it is decolorized.

M. cereus albus.—Found in pus, singly or grouped, not motile, $1.15\ \mu$ diameter. Small white colonies on plates, superficial waxy streak in gelatine and agar tubes with edges elevated, also on serum and potato; grows at $30-37^{\circ}\text{C}$. and does not liquefy gelatine. Causes suppuration, usually associated with other forms.

Stains, with usual methods.

M. cereus flavus differs from last by producing yellow pigment.

FIG. 57.



STREPTOCOCCUS PYOGENES. (*Stengel.*)

Streptococcus pyogenes.—Found in pus and erysipelas, not motile, in linear series of 20-40 cocci, $0.4-1.0\ \mu$ diameter, aerobic.

Culture.—Gelatine. On plate, colonies small, round, granular, brownish, edges raised; middle sunk; non-liquefying. Superficial growth in tubes. Agar about the same. Grows slowly at 37°C . and is apt to die out.

Pathology.—Alone or with other cocci it is found in suppurations, erysipelas, malignant endocarditis, otitis; often associated with diphtheria and tuberculosis.

Stain, usual dyes; G. +.

M. tetragenus.—Found as saprophyte in lung diseases of man, not motile, in pairs and fours, facultative aerobic. Grows as small white granular colonies on plates; on agar, serum and potato, heavy white film. Kills mice and guinea-pigs, not rabbits or field mice.

Stains, with usual dyes; G. +.

Diplococcus of Pneumonia.—Found in sputa of lobar pneumonia, exudate of meningitis, at times in saliva of healthy persons, non-motile, aerobic, 2-6 in series with common capsule which is lost in culture media.

Culture.—Gelatine. Small white, sharp-edged colonies, not liquefying; on agar almost invisible; on serum, transparent moist film. T. 24-42°, best 37° C.

Pathology.—Probably the cause of croupous pneumonia, but has been found in joint lesions, serous inflammation and meningitis.

Stain, usual dyes; G. +.

Diplococcus intracellularis of Meningitis.—Found in exudate of epidemic meningitis, not motile, in pairs, fours and short chains, aerobic.

Culture.—Does not grow on gelatine or potato, scanty in beef broth and on agar, best on blood-serum mixture forming very small colonies, smooth and round but may coalesce; requires frequent transplanting. T. 36° C.

Pathology.—Causes epidemic cerebro-spinal meningitis; pathogenic for dogs and small rodents.

Stains, usual; G. —.

Diplococcus of Gonorrhea.—Found in cells of gonorrheal inflammation, both in protoplasm and nucleus of pus cells, in lesions of urethral mucous membrane, joints, etc., in this disease; not motile, aerobic, arranged usually in twos with slightly concave surfaces opposed, 0.8-1.5 μ diameter; when its virulence is attenuated it is found outside of the cells and is called pseudogonococcus.

Culture.—Not on gelatine. On human blood serum, smooth,

thin, gray or yellow film, edges become more clearly distinguishable later, very slow; on albuminous urine and acid gelatine also; surrounding the colony there may be irregular ill-defined extension. T. 37° C. ($25-38^{\circ}$ C.).

FIG. 58.



GONOCOCCI. (PHOTO.)

For the most part enclosed in pus cells.

Pathology.—Causes catarrhal, suppurative inflammation of mucous membranes; has been found in joints and in heart (malignant endocarditis), pyo-salpinx, peritonitis, conjunctivitis.

Stain, usual; G. —.

Diplococcus of Trachoma.—Found in lesions of trachoma, usually in pairs, like gonococcus but smaller and less distinct, not motile, aerobic. Grows as a shiny film on most media with little beads along the stick; not liquefying. T. 35° C.

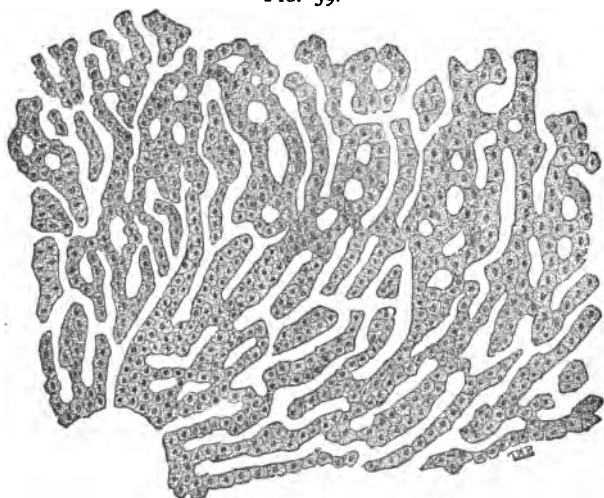
Other cocci have been found in certain skin diseases, as pemphigus, pityriasis rosea, etc., and many forms among lower animals both resembling and differing from those in man.

Pathogenic Bacilli.

Anthrax.—Found in blood of animals infected, not motile, aerobic and facultative anaerobic; rods with square ends, $1-1.25 \mu$ broad by $3-20 \mu$ long, single, grouped and in filaments.

Culture.—Grows on all media, as a film on potato, in tree form in gelatine stab; liquefies both gelatine and serum. T. 12–45° C., best 37° C.; spores formed toward the higher limit in cultures, never in the blood. Colony peculiarly marked by wavy lines which start from edge and return, like locks of hair displayed. Very resistant, especially the spores.

FIG. 59.



BAC. ANTHRACIS IN LIVER. (Delafield and Prudden.)

Pathology.—Cause of anthrax carbuncle, malignant pustule and wool-sorter's disease in man; charbon, splenic fever in herbivora.

Stain, usual; G. +.

Anthrax, Symptomatic.—Found in body fluids of infected animals, motile, flagellate, anaërobe, delicate rods singly and paired, 0.5 μ broad by 3–5 μ long, ends round.

Culture.—All media. Liquefies gelatine, appears as irregular granular colonies with thick center and radiate branches, in stab forms gas. T. 13–70° C., best 37° C.

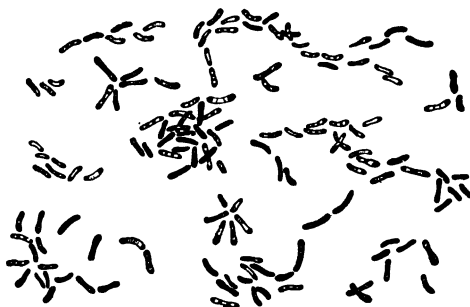
Pathology.—Cause of symptomatic anthrax, man and animals.

Stain, usual ; *G.* imperfectly.

B. coli communis.—See typhoid.

B. diphtheriæ.—Found in the membrane, not motile, aërobic, facultative anaërobic, rods straight or a little curved, $0.3-0.8\ \mu$ broad by $2-4.5\ \mu$ long, stain markedly at the ends.

FIG. 60.



BAC. DIPHTHERIÆ. (Stengel.)

Culture.—Usual media ; on potato hardly visible for a time, then a thin dry film with resistant feel ; in gelatine stab small colonies form along the stick and join to make a gray line ; best medium blood serum ; milk, agar and alkaline broth also. On serum in 6–24 hours a thin white layer forms, sometimes a little yellowish, with minute colonies near the edge. T. $20-40^{\circ}+$, best 37° C.

Pathology.—Causes inflammation of varying severity on mucous surfaces and wounds with production of false membrane, made of fibrin chiefly, with bac. diphtheriæ in its meshes, associated with strepto- and staphylococci usually, so that the effect on the organism is of a mixed infection. After recovery the bacillus persists in mouth and nose for weeks ; attenuated forms called pseudo-diphtheria bacilli.

Stain, usual, especially Löffler's methylene-blue ; *G.* +.

B. influenzae.—Found in mucus and discharges from nose and bronchi of infected persons, less often in blood, not motile, aërobic, in twos or short chains, $0.4\ \mu$ by $0.8-1.2\ \mu$, sensitive.

Culture.—Grows with difficulty on agar streaked with fresh sterile blood, as very fine drops like dew. T. 28–60°, best 37° C.

Pathology.—Cause of influenza in man and monkeys. A similar organism has been isolated from the lung of post-diphtheritic pneumonia.

Stain, usual; G. —.

FIG. 61.



BAC. EDEMATIS MALIGNI. (Stengel.)

B. edematis maligni.—Found in garden earth, intestines of normal animals and connective tissue of infected animals, perishes in blood; motile, anaërobic, rods 3–5.3 μ long by 1 μ broad, ends rounded, may form long series.

Culture.—Grows on usual media, liquefies gelatine, on agar plate grows in the deep layers as white opaque spots; in gelatine stab forms white cloudy colonies and gas, especially if glucose is present. T. best 37° C.

Pathology.—Cause of malignant edema, cattle nearly immune, cat and dog less so, small rodents very susceptible. Not found in the blood till long after death because of oxygen in it.

Stain, usual; G. —.

B. pneumoniae.—Found in sputa and lung of croupous pneumonia, not motile, aërobic, rods short enough to resemble cocci or longer, often in short chains with a common hyaline capsule, measurements uncertain.

Culture.—All usual media. In gelatine stab makes a characteristic nail-shaped figure; forms gas, does not liquefy gelatine. T. 14–40° C., best 37° C. Spores?

Pathology.—May cause croupous inflammation in man, dog, guinea-pig.

Stain, usual; G. —.

B. pyocyaneus.—Found in green pus, motile, aërobe, rods 0.5 μ by 1.5 μ , grows on gelatine, potato, agar, milk; liquefies

gelatin; on solid media makes transparent film in 24 hours, which turns greenish and medium fluorescent. T. best 26–37° C.

Pathology.—Causes a green color in pus, may produce septicemia as it is virulent in pure culture.

Stain, usual; G. +.

B. pyogenes fetidus.—Found in foul pus, motile, aërobe, short rods with rounded ends, singly and chains, 0.5 μ by 1.4 μ . Grows in broth and on solid media as light gray film turning brown as it becomes thicker, shiny, rapid grower, odor disgusting, does not liquefy gelatine. T. 30–37° C. Fatal to small rodents.

Stain, usual; G. +.

B. pestis.—Found in lymph nodes, spleen, blood and feces of patients dying of bubonic plague, flagellate, motile, aërobe and facultative anaërobe, 1.7 μ by 2.3 μ , swollen and staining on ends, gives appearance of diplococcus.

FIG. 62.



BAC. TETANI. (Stengel.)

Culture.—Various media, glycerine agar makes white or blue-white colonies; in gelatine stab makes tree form, does not

liquefy it; best medium alkaline peptone with two per cent. gelatine; forms acid and indol; in presence of salt (3 per cent. NaCl) at 37° C. forms yeast-like involutions.

Pathology.—Cause of bubonic plague in man, fatal to small animals, spread by rats and flies.

Stain, usual; G. — .

B. tetani.—Found in earth which has been manured and in discharges of wounds after infection; motile except with spores, anaërobic; in straight rods, racket and spindle shapes and chains, 0.5–0.8 μ by 1.2–3.6 μ , many involution forms.

Culture.—Best, alkaline gelatine with 2-per-cent. dextrose, also on agar, serum, and in broth; liquefies gelatine, forms gas; in depth of gelatine stab single colonies form at right angles to stick; end spores common and resistant. T. 14–42°, best 36–38° C.

FIG. 63.



BAC. TYPHI WITH FLAGELLA. (*Stengel.*)

Pathology.—Cause of tetanus in man, fatal to mouse, rabbit, guinea-pig.

Stain, usual; G. + .

B. typhi abdominalis.—Found in water and milk from contact with infected person ; urine, feces of the sick ; spleen, intestine and gall bladder of the dead ; motile, flagellate, aërobic, facultative anaërobe, single or grouped, straight rods with round ends, $0.5-0.8 \mu$ by $1.0-3.0 \mu$ long.

Culture.—Potato, agar, gelatine, serum, milk, not liquefying. On potato characteristic invisible film, moist and shiny, resistant to touch. T. $15-45^{\circ}$ C., best 37° C.; spores form at $30-42^{\circ}$, one in each rod, at the end.

Pathology.—Cause of typhoid fever in man ; after alkalinizing the stomach and arresting peristalsis in animals, feeding with typhoid cultures causes intestinal lesions ; injected into the blood causes septicemia.

Stain, usual ; G. —.

Chief differences between *b. typhosus* and *b. coli communis* :

	B. TYPHOSUS.	B. COLI COMM.
Colonies on gelatine plates.	On surface large, gray-white, edges irregular, turn yellow brown ; in the depth, dark with regular edges ; non-liquefying.	Colonies dirty white, turn dirty yellow, round or oval, margins smooth ; non-liquefying.
Potatoes.	Faint gray white film on acid potato usual.	Growth slimy and yellow.
Milk.	Acidulated, not coagulated.	Acid reaction, coagulated in one to three days.
Broth.	Becomes turbid, no indol.	Turbid, indol in 24-48 hrs.
Widal reaction.	Positive with blood from typhoid patient or animal immunized.	Negative.
Suppuration.	Sometimes in post-typhoid abscesses, as of parotid.	More strictly pyogenic.

Otherwise resemblance is close and identification difficult.

B. mallei.—Found in farcy buds, mucous discharges and exudates of infected man or animal (especially horse and ass), slight motility, aërobe, facultative anaërobe, rods like tubercle bacilli but shorter and thicker, 0.4μ by $2-3 \mu$ with irregular staining simulating spores.

Culture.—Potato, makes yellow slimy film, honey-like, turning browner; on gelatine round dots with undulating margin; on agar scattered honey-like drops. T. 25–42° C., best 37° C.

Pathology.—Causes glanders and farcy in animals, transmissible to man and rodents.

Stain, usual, especially alkaline solutions, needs a long time with quick decolorization; G. —.

Rhinoscleroma Bacillus.—Found in nose and throat of infected individuals, in the tissue, not motile, facultative anaërobe, short rods with ends rounded, some like oval cocci, single, paired and chains, 0.5 μ by 1.5 μ .

Culture.—Forms white layer on usual solid media, non-liquefying; in stab makes nail figure but the head is transparent. T. best 36–38° C. Retains its capsule in culture media.

Pathology.—Cause of rhinoscleroma; no effect on animals.

Stain, usual; G. +.

B. aërogenes capsulatus.—Found in fluid of tissue destruction in emphysematous necrosis and gangrene, not motile, anaërobic, rods like anthrax, ends square or rounded, 1.0–1.25 μ by 3.0–6.0 μ , pairs, clumps and short chains, capsuled in agar at times, no spores.

Culture.—Deep in agar and gelatine stabs as small lenticular disks with knobs or feathery projections, white or gray, forms gas, liquefies gelatine slowly; T. 36–40° C.

Pathology.—Causes emphysematous gangrene, found in the cadaver early in decomposition; may explain “air embolism” of the lung after parturition.

Stain, usual; G. +.

Pathogenic Spirilla.

Cholera asiatica.—Found in “ricewater” feces and intestinal contents of infected persons, motile, with end flagellum, aërobe and facultative anaërobe, in short arcs and spirals, “comma” forms, or longer winding filaments, 0.5 μ by 0.8–1.5 μ , no spores.

Culture.—Usual culture media, liquefies serum and gelatine; on plate forms white or yellow-white colonies with granular surface and irregular margin; in gelatine stab liquefaction begins at surface and proceeds downward, making inverted cone with

FIG. 64.

PETRI AGAR PLATE. (*Delafield and Prudden.*)

Made by spreading scrapings from the mouth over sterilized nutrient agar; after 48 hours in the thermostat the light "colonies" develop.

air bubble at top; in broth and liquid media forms indol and nitrites, giving "cholera red" reaction with pure HCl or H_2SO_4 ; milk not coagulated. T. 14-42° C., best 37° C.

Pathology.—Cause of Asiatic cholera in man ; similar lesions in animals after neutralizing the gastric juice and arresting peristalsis.

Stain, usual ; G. — .

FIG. 65.



SP. CHOLERÆ ASIATICÆ. (*Stengel.*)

Spirilla resembling that of cholera asiatica.

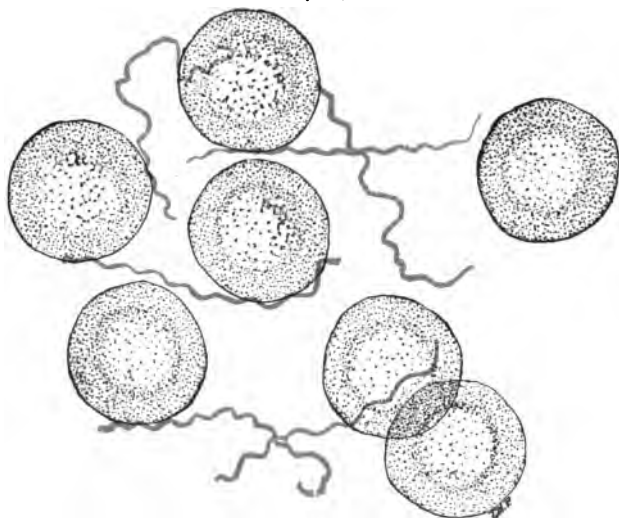
Finkler-Prior ; obtained from feces of cholera morbus, like former in shape, growth and indol formation, but longer, more slender ($0.5-0.6\mu$ by $0.6-2.5\mu$) and coagulates milk ; in gelatine stab grows faster and liquefies faster ; motile, with end flagellum.

Deneke's tyroginicum. Found in old cheese ; liquefies gelatine faster than *s. cholerae* but not so fast as Finkler's ; motile, end flagellum.

Spirillum of Metschnikoff, found in feces of hen cholera, shorter and thicker than cholera asiatica, but cultures very similar ; not pathogenic for man ; kills chickens, pigeons and guinea-pigs.

Spirillum sputigenum, isolated from saliva, resembles cholera, but longer and thinner; not cultivated in any medium so far.

FIG. 66.

SPIROCHETE OF RELAPSING FEVER. (*DeLafield and Prudden.*)

Spirillum of febris recurrens.—Found in blood of patients with relapsing fever during the paroxysm, vanishes afterward; very motile, undulating pliant filaments with pointed ends, $0.1\ \mu$ by $20\text{--}35\ \mu$ or longer, spirally twisted, no spores.

Culture.—Not yet propagated outside the body.

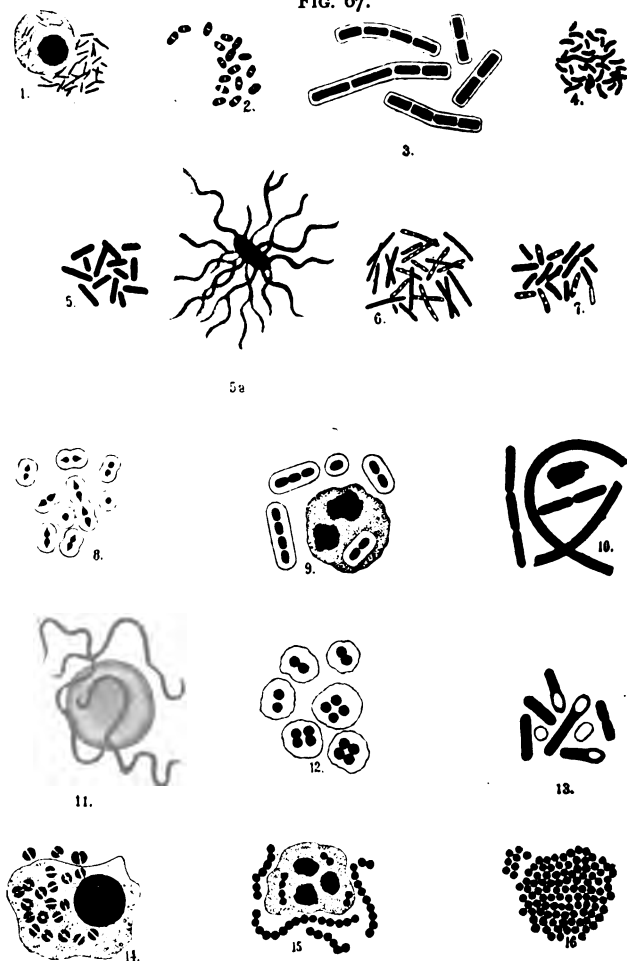
Pathology.—Constant in relapsing fever; transmissible to monkeys by injecting blood of patient.

Stain, usual; G. —.

Organisms of Infectious Granulomata.

Bacillus of Leprosy.—Found in skin and other lesions of leprosy, not motile, rods like tubercle bacilli, but ends sharper and take basic stains better, $0.5\ \mu$ by $4.0\text{--}6.0\ \mu$; spores?

FIG. 67.

PLATE OF BACTERIA ON THE SCALE OF 1 TO 1,600. (*Birch Hirschfeld.*)

1, bacilli of swine erysipelas; 2, bacilli of hen cholera about a red cell, from fowl's blood; 3, anthrax bacilli with capsule; 4, cholera vibrio; 5, bacillus typhosus; 5a, the same with flagella; 6, tubercle bacilli; 7, glanders bacilli; 8, pneumococcus of Fränkel; 9, bacillus pneumoniae of Friedländer; 10, bacillus of malignant edema; 11, spirochete of relapsing fever; 12, micrococcus tetragenus; 13, tetanus bacilli with end spores; 14, gonococci; 15, streptococci; 16, staphylococci. The relative size of the organisms appears from the ac-

Culture.—Not yet successfully grown on artificial media.

Pathology.—Constant in leprosy of all forms.

Stain, usual, but with difficulty; G. +.

Bacillus of Syphilis.—Described as found in most lesions and exudates of syphilis, resembles tubercle bacilli, but, like the lepra organism, cannot be cultivated or transmitted to animals; causal relation to syphilis questionable. A similar bacillus found in secretions from Tyson's glands (smegma).

Bacillus tuberculosis.—Found in sputa and lesions of tuberculosis, non-motile, aerobic, rods straight or curved, ends rounded, $0.25\ \mu$ by $1.5\text{--}3.5\ \mu$, sometimes present oval unstained areas which suggest spore formation, branching forms have been found, closely resembles a rod bacillus from cow dung, as also the timothy hay bacillus.

Culture.—On potato, serum, glycerine agar, in glycerine broth and milk; growth slow; on glycerine agar small white dots which join later to form "bread crumb" layer, wrinkled yellow-white film; more yellow on potato. T. $30\text{--}42^{\circ}\text{C}$., best 37.5°C .

Pathology.—Cause of tuberculosis in man, all forms; may be transmitted to many lower animals. Whether the bacilli from tuberculosis in animals are pathogenic for man is still disputed.

Stain, usual and special methods, Ziehl-Neelsen quick and satisfactory; G. +.

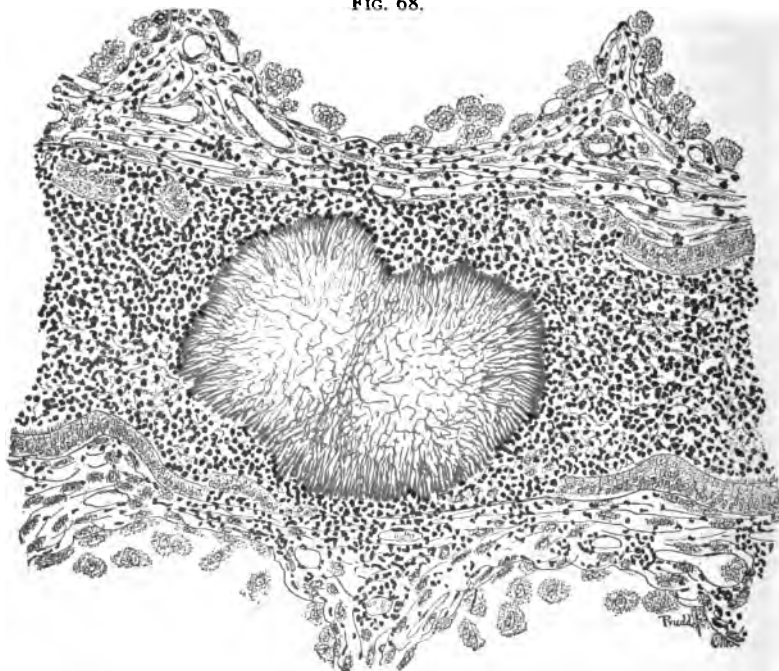
Actinomycosis; Ray Fungus.—Found in lesions of the disease in man and animals, not motile, both aerobic and anaerobic, in three forms:

1. Coccus, $0.5\ \mu$ diameter, perhaps the spores of
2. Long threads, slender or thick, often curved, may be slightly thicker on ends, not clubbed; anaerobic.
3. Filaments distinctly club-shaped, radiating from a center which in tissues is often calcified.

Culture.—Anaerobic alone pathogenic. On serum forms a thin gray, moist layer, made of fine transparent lines, parallel or

woven ; in 24 hours air hyphæ project and give the appearance as if sprinkled with chalk ; as culture dries the white spots turn reddish-yellow or rusty, T. 33–37° C., with exclusion of oxygen.

FIG. 68.

ACTINOMYCES. (*Delafeld and Prudden.*)

Pathology.—Cause of actinomycosis in animals, less often in man.

Stain, yellow with iodine and picric acid, red with picrocarmin, blue with aniline gentian, cocci red with eosin ; G. +.

APPENDIX TO CHAPTER IX.—IMMUNITY.

Certain people, though exposed to infection by various disease-producing bacteria, appear but little liable to the attack, others

who have had a disease may never have it again even when exposed ; such resistance to disease is called immunity and may be natural, as where certain races of men or animals are less apt to take disease than others (the negro in some yellow-fever epidemics); or acquired, when susceptibility gives place to resistance. This acquired immunity may be either active or passive.

Active immunity follows an attack of a certain disease and secures immunity for that alone, which may last but a short time (erysipelas, cholera) or for a longer period (typhoid), or even for life (variola); or it follows inoculation of a virus weaker than necessary to cause the typical disease (vaccination against small-pox); or it follows inoculation by bacterial products apart from the organisms themselves. Passive immunity is the term applied to the effect of a serum derived from an immunized animal and injected into one not immune, the theory being that in the blood of the former there is a chemical substance (antitoxin) which neutralizes the toxin in the donating animal, or otherwise it would show symptoms, and by borrowing its serum for the infected animal the toxin is opposed by the alien antitoxin. A local immunity is spoken of, but the term is of doubtful value.

THEORIES OF THE MODUS OF IMMUNITY.

1. The bacterial products accumulate in the infected organism to a percentage which inhibits further activity or growth (Chauveau).
2. The cells which have combated the agent of infection with success acquire and retain increasing power of resistance (Grawitz).
3. The germs having special localities of attack, the cells there develop resisting powers for the particular germ in question (Buchner).
4. The ameboid cells have the power of ensphering bacteria and digesting them ; part of the ingested organism is returned to the serum in harmless form and excreted ;

the white cell breaks up (phagolysis) and sets free in the stream its resisting chemical element. The cells (phagocytes) thus "eating" bacteria are:

1. Micro-phagocytes; eosinophile and amphophile.
2. Macro-phagocytes; large lymphocytes.
3. Endothelial cells, of capillaries.
4. Fibroblasts.
5. Pseudo-plasma cells. (Metschnikoff: Phagocytosis.)

As a matter of fact the phagocytes may take bacteria to places which they would not otherwise reach and there set them free to attack tissue: as when a non-motile tubercle bacillus is carried from the bronchial mucous membrane to a lymph node, or from the surface of a Peyer's plaque into the lymphoid tissue.

5. The fresh blood serum contains chemical bodies (alexins) which destroy bacteria; now extended to include various tissue fluids. These defensive substances, supposed to be proteids, are called sozins if naturally present in the serum, phylaxins if the result of immunization; the former destroy both blood cells and bacteria and are themselves destroyed by exposure to 55° C.; if they oppose the bacterium they are called myco-sozins, and if they counteract the toxin, toxo-sozins. The phylaxins, the true antitoxin, destroy neither blood cells nor bacteria and retain their properties after exposure to 80° C.; they also are divided according to their activity into myco- and toxo-phylaxins (Buchner-Hankin).
6. The blood contains three bodies—toxin, toxoid and toxone; each toxin element is compound, made up of combining elements (haptophore) and poisonous bodies (toxophore). The toxin is the important member of the group, having poisonous properties, but as it com-

combines with more antitoxin than one would expect it must contain also the non-poisonous haptophores. The older the serum is the less its poisonous power, through conversion of toxin into toxoid, though the combining power may persist unchanged. The toxone is also a bacterial product in addition to toxin, less poisonous but able to combine with antitoxin. A toxin introduced into the blood combines by its haptophore elements with some element in the cells of the body, and having thus made its way into the cell protoplasm the toxophores are able to attack it. In other words, the haptophores resemble the clasping claws of an alien organism which facilitates a direct attack by its teeth or other offensive weapon. Just as in organic chemistry the benzole ring persists despite changes in the side chains, so do the toxophore elements remain active while the haptophores enter into combinations; and after the haptophores excite the cell to combine, because of the consequent destruction of the cell such combinations are liberated to functionate in the serum as antitoxins. Invading organisms vary in their ability to select and combine with special body cells and thus form antitoxin, but obviously those which attack cells of highly specialized function (tetanus action on nerve cells) demonstrate the greatest and most pernicious activity. (Ehrlich : Side Chain.)

The entire subject is as obscure as it is of practical interest.

CHAPTER X.

INFECTIOUS DISEASES.

WHEN microörganisms enter the body, proliferate and cause disease, the act is called infection and the disease infectious. Bacteria may cause local effects, stopping small vessels or setting up productive or degenerative cell and tissue changes; they gain entrance usually through some solution of the body coverings, cutaneous or epithelial. Their constitutional effects may be due to the absorption and distribution of their products alone (intoxication, as tetanus), or the bacteria may invade every tissue or selected parts (true infection, as anthrax). The terms toxemia for the former and septicemia for the latter are often used for these conditions. Infection may be congenital; tuberculosis, syphilis and anthrax sometimes pass from mother to child via the placenta. Terminal infection is the unusually rapid and hence fatal invasion of a patient already weakened by some disease. Mixed infection is seen where two organisms coexist in the tissues, as diphtheria and streptococcus, tubercle bacilli and pus organisms. Many of the infectious diseases are communicable directly from man to man (scarlet fever), others through an intermediate organism (malaria, yellow fever), others apparently not at all (tetanus). When bacterial products occur in the blood, the condition is called sapremia; if pus organisms occur in the blood without producing secondary pus foci, septicemia; if present and causing multiple abscesses, pyemia.

Pathogenic Bacteria as the Cause of Disease.

The Pus Group.—Beside the usual pus organisms, strepto- and staphylococci, many other bacteria are positively tactic to pus

corpuscles and wherever they lodge set up suppuration, locally as boils, pustules and abscess and generally as suppurations of joint surfaces and serous membranes. They often play a part as the second element in mixed infections, as in tuberculosis of the lung, where there is no cavity formation and little fever or emaciation until the action of pus organisms is marked in tissues already weakened by tubercle bacilli. Pus confined in the tissues gives rise to intoxication through absorption of toxin and that from streptococci is specially virulent. Other pus organisms are *b. coli communis*, *b. pyocyaneus*, *b. proteus*, *diplobac. pneumoniae*, etc. A special form of disease due to a coccus is erysipelas, the organism of which appears to be identical with *streptococcus pyogenes*.

Post-mortem Changes after Septicemia and Pyemia.—There may be no gross lesion; the chief finding may be remarkably rapid decay of all the tissues, hemorrhages passim, general congestion of all organs, softening of the spleen and post-mortem staining by blood coloring matter; abscesses may occur in many organs and in the joints, with pus on serous membranes; there may be venous thrombi at the seat of the primary pus focus and multiple emboli of infected material.

Epidemic Cerebro-spinal Meningitis.—An acute suppurative inflammation of the meninges of brain and cord, especially the pia, serum, fibrin and pus present in varying amounts, over the whole cortex and throughout the cord, or localized or so scanty that the microscope is required to detect the exudate. Fluid obtained during life by puncture of the lumbar spine may contain cells with the *diplococcus intracellularis* inside; the usual pus forms and *pneumonia diplococci* have also been found. Other lesions are hemorrhages in skin and serous membranes, abscesses in joints, degenerations in voluntary muscles and cloudy swelling of parenchymatous organs.

Croupous Pneumonia.—The *diplococcus pneumoniae* is often a cause of lobar pneumonia but not the only one. It may occur in the healthy mouth and lung and has been the ap-

parent cause of pleuritis, otitis, meningitis, peritonitis and other suppurative diseases. For gross and microscopic appearances see Part II.

Gonorrhea.—This disease is caused by the diplococcus known as gonococcus and is an acute, very contagious inflammation of exudative type affecting mucous and serous surfaces. Beside the changes in the urethra, this organism has caused inflammation of the conjunctiva, peritoneum, joints, endocardium and fallopian tubes.

Anthrax.—Splenic fever or malignant pustule is rare in man in the United States. The germ gains entrance through skin abrasions and by inhalation and causes local or general effects. Post-mortem decomposition is rapid, blood not much coagulated, bleeding common on surfaces, edema or inflammation of lung, spleen swollen and soft; microscopically the bacilli are found in numbers in capillaries of liver, kidney and lung.

Diphtheria.—The false membrane may be found on mucous surfaces of the upper air passages or in the bronchi and stomach; it is formed of fibrin, pus, epithelia and red cells, with diphtheria bacilli and pus organisms, and under it the tissues may be necrotic; or there may be no membrane, the mucous surfaces being simply congested and inflamed. Where the false membrane has sloughed off there may be ulceration, the lymph nodes are swollen or softened, parenchymatous organs present foci of necrosis, nephritis is usual, degeneration and inflammation of the nerves common.

Influenza.—Post-mortem appearances are not typical, being those of the fatal complication, very commonly pneumonia.

Bubonic Plague.—The characteristic lesions are swollen and suppurating lymph nodes, especially of groin and axilla, but in some cases there are no buboes, only the lesions of fatal intercurrent disease, as lobar pneumonia; the punctate hemorrhages common to all diseases with fever and disorganization of the blood are also present, with blood-stained serum in the body cavities.

Tetanus.—The central nervous tissues are apt to be intensely congested and the wound which was the port of entry may be found ; microscopically intense active hyperemia of the cerebral capillaries with cellular exudate in the perivascular spaces and degeneration of ganglion cells. The bacilli occur only at the wound ; sometimes when there is no evident wound it is assumed that they enter through the alimentary or other mucous membrane. In tetanus neonatorum the wound is the cut surface of the cord.

Typhoid having so distinct a lesion in the intestine will be treated in Part II., Chap. IV., but there are cryptic cases where the intestinal lesion fails (as with intra-uterine infection), and in any case the more distant lesions may be very marked, as splenic and hepatic necrosis, parotic abscess, degeneration of voluntary muscles, etc.

FIG. 69.

GLANDERS, GROSS LESION. (*Birch Hirschfeld.*)

Acute infection by bacillus mallei. Ulceration developed in 8 days from pemphigus-like vesicles.

Glanders.—The lesions are chiefly located about the upper respiratory tract, elevated areas on the mucosa of the nose which soften, ulcerate and join to form extensive loss of tissue, with yellow necrotic floor and purulent discharge ; similar nodules in larynx and lung and at times in the alimentary canal ; boils, car-

buncles and abscesses occur in the skin and between the muscles, and nodules are found in spleen, liver, testes, etc.; osteomyelitis and joint suppurations occur. When small these nodules resemble miliary tubercles. "Farcy buds" occur in the skin, especially when an abrasion is the point of entry. Microscopically there is an infiltration of small leucocytes, proliferation of epithelioid cells, hyperemia and rhexis, necrotic changes and softening, and near mucous surfaces, increased production of altered mucus which excoriates the skin adjacent.

Rhinoscleroma presents nodular thickening of the tissues of the nose and adjacent parts, the lip, pharynx and larynx, associated with ulceration of the mucous parts involved. Microscopically the new tissue resembles granulation tissue, and between the cells are the bacilli, which occasion hyalin degeneration also; since the disease cannot be reproduced in animals the exact relation of the bacillus is undetermined.

Cholera Asiatica.—The chief lesions are those of the alimentary canal and will be treated in Part II., Chap. IV.

FIG. 70.



LEPRA BACILLI IN THE LARYNX. (Birch Hirschfeld.)

Relapsing Fever.—Beside the presence of the spirochete in the blood there are no characteristic lesions; the tissues may be jaundiced, parenchymatous organs may be softened and degen-

erated, especially the spleen, which may be large and soft enough to rupture before death or may contain infarcts, and abscesses from their softening; and other lesions associated with high temperature occur, submucous ecchymoses, etc. Changes in the long bones, both degenerative and productive.

Variola.—The post-mortem appearances are those of the dermatitis, macule (seldom persists), papule, vesicle, umbilicated vesicle, pustule, scab and ulcer; and those of fever and pus infection, various bleedings, degeneration of organs, and inflammation of mucous membranes, severe streptococcus infection is always present.

Rabies, typhus, pertussis, scarlet fever, measles and yellow fever have no constant and characteristic post-mortem changes, and the lower organisms which undoubtedly cause them are still to be discovered.

The Infectious Granulomata.

Lepra Arabum, Elephantiasis Grecorum, Leprosy.—Infectious disease of chronic course, characterized by the formation of granulation tissue under the influence of the lepra bacillus, in conditions of bad sanitation; the skin shows tumor-like nodes (*l. tuberosa*) or patches (*l. maculosa*), the nerves are apt to be involved (*l. anethetica*). The face is often attacked early, hyperemic spots appear and fade again but for some pigment, or swell into nodules, arranged singly, in groups, or confluent; composed of small and large round cells, especially about the hair-follicles and reaching into the subcutaneous tissue, with stellar and spindle cells associated; the adjacent tissue atrophies, the nodules persist for a time, then soften and form ulcers. Such nodules may occur on the back of the hand (*palm exempt*), the extensor aspect of joints, and in mouth, tongue, gum, larynx, etc. Adjacent lymph nodes are apt to be swollen, hard and yellow, from connective-tissue hyperplasia and fatty degeneration of the cells. Fever may accompany the formation of new nodules, nephritis is common, tubercle infection often oc-

curs late in the disease, amyloid changes are found in ulcerating forms. The disease may last ten years or more before ending fatally. Liver, spleen and testis may present diffused or localized connective-tissue hyperplasia. The lepra bacilli are found

FIG. 71.

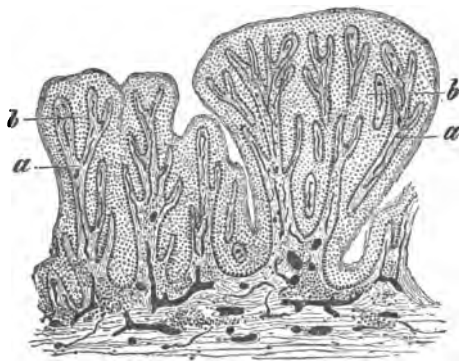
NODULAR FORM OF LEPROSY. (*Birch Hirschfeld.*)

in all affected tissues and in the endothelium of the vessels, free and in cells, giant and others. The disease is said to be hereditary and contagious, but slightly in each case, seldom appears till after the third year of life, most common in males from 20 to 30 years, and in the United States only among immigrants.

Syphilis.—The disease is peculiar to man and consists of a local initial lesion, the chancre, with constitutional symptoms,

after the lapse of some weeks usually, followed by secondary and even tertiary constitutional changes with long intervals between. The initial sore may be an eroded papule or an ulcer on an indurated base, associated with moderate swelling of the corresponding lymph nodes, made up of small round-cell infiltration, connective tissue proliferation and hyaline change in the vessel walls and tissue about them, with more or less complete obliteration of their lumina; the proliferation and hyaline changes are the essential ones, inflammatory follow. The chancre may occur on any surface of the body within reach of the virus, but in the majority of cases it is found on the external genitals. The

FIG. 72.



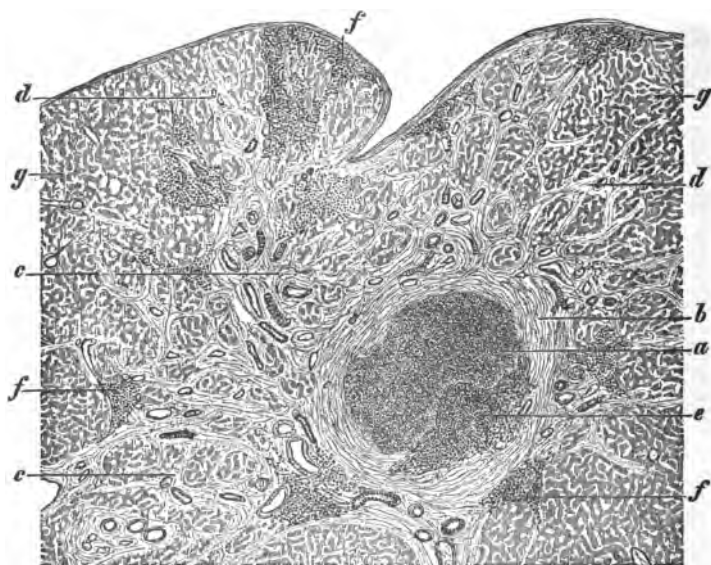
CONDYLOMA ACUMINATUM. (Ziegler.)

a, enlarged branching papillæ; *b*, epidermis, reaching to the bases of the hypertrophied papillæ.

secondary lesions are varied, most commonly a skin eruption with fever, constitutional disturbance, and anemia from destruction of red cells and increase of white; condylomata, local elevations of the skin due to the irritation of secretions, often about the perineum, consisting of marked infiltration of the papillæ and epidermis with round cells, accompanied by edema, plasma cells abundant; these lesions occur as long as 6-8 weeks after the chancre. In some cases, usually after two years, tertiary

changes occur, involving bones and viscera, consisting of tumor-like connective-tissue growths with a tendency to caseous and other degeneration—the syphilitic gumma. In the gross such gummata are hard and dense, made up of a band or series of bands of fibrous tissue enclosing dry, caseous masses, often several, with indications of a wide meshwork between; through softening and absorption only an irregular scar may be left. Micro-

FIG. 73.



GUMMA OF THE LIVER. (Ziegler.)

a, Caseous nodule; *b*, connective tissue, at *c*, enclosing atrophic liver cells, at *d*, radiating into the liver parenchyma; *e*, cellular foci at edge of caseous nodule and in fibrous bands, at *f*; *g*, liver tissue.

scopically the remains of cells and nuclei are found in a granular fatty mass; the vessels of the part are narrowed or closed by proliferation of the intima, round and spindle cells may appear in the adventitia, the media is less often involved. Giant cells may be found. Such gummata in bone (skull, tibiae),

may soften and destroy them ; they are common in liver, testis, spleen and brain. The fetus may be attacked before birth and die in utero, or if born alive falls a victim to diarrheal diseases ; the upper incisors of the second dentition are notched on the free edge, other teeth may be imperfect, conical and peg-shaped. Gummata may occur in these children even when dying in the first week, and they may be soft, small and in beginning necrosis or already caseous. Other lesions are pneumonia, induration of spleen and pancreas, hyperplasia and fatty degeneration of the long bones at the epiphyseal lines, and skin lesions.

FIG. 74.

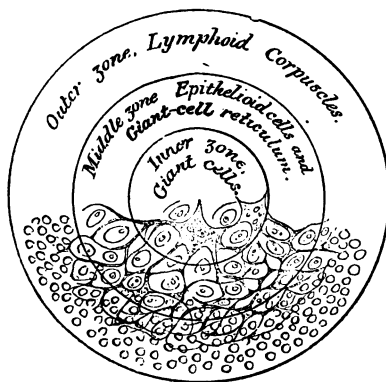
TUBERCLE BACILLI IN GIANT CELLS. (*Birch Hirschfeld.*)

From chronic peritoneal tuberculosis.

Tuberculosis.—The name tubercle, applicable to any small nodule, is now reserved for the result produced by tubercle bacilli in the various tissues ; distinctions of color, white, gray or yellow tubercle, are not considered of importance at present ; the smallest tubercles are called miliary, larger are conglomerate, but any tubercle visible to the naked eye is made up of smaller groups, each called a granuloma ; tissue not presenting

nodules but containing much tubercle tissue is said to be infiltrated. Histologically the tubercle is a collection of epithelioid cells with large oval nuclei and glistening nuclear bodies; between these cells there is a delicate fibrillar basement substance which is more apparent in older forms; in many tubercles there

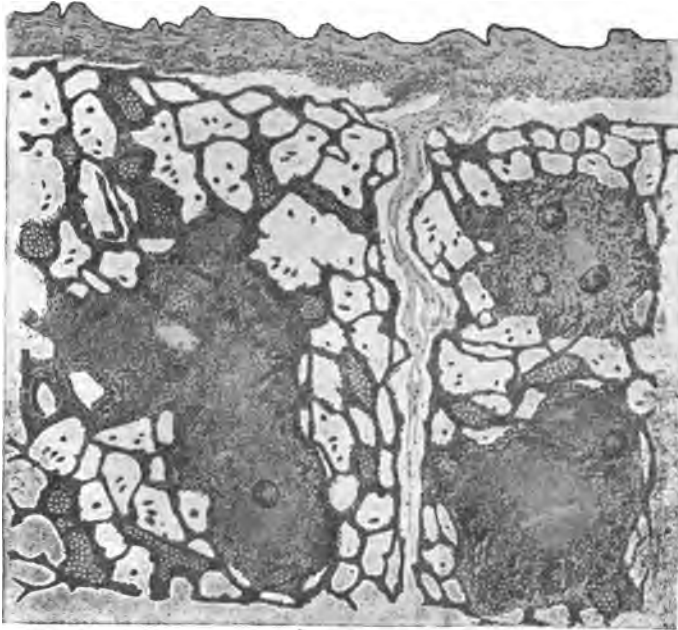
FIG. 75.

DIAGRAM OF TUBERCLE. (*Coplin.*)

are also giant cells, which occupy the central zone, round or oval, sometimes with processes, containing 20-100 oval or round nuclei, which in old giant cells are arranged in a chain about the periphery; external to these elements there is often a zone of lymphocytes, especially in acute forms of tuberculosis. In chronic cases the center of the tubercle regularly undergoes cheesy (caseous) degeneration, becoming dry, not staining, with coarse or fine granules scattered throughout, or the contents may be softer and creamy, and about the tubercle there may be a new formation of connective tissue shutting it off from the other tissues, with calcification of the fibrous capsule. Or new fibrous tissue in strands may be distributed through the tissue, enclosing tubercles here and there, or in bones and joints the formation may be spongy and fungus-like. On mucous mem-

branes there may be warty or papillary growths as also in the skin (usually known as lupus). The giant cells and the epithelial elements may come from the lymph-vessel endothelium, the adventitia of small blood-vessels, from fibro-blasts, or from leucocytes which wander into the tissue in response to the products of the bacilli (cytotaxis). Carried elsewhere from such a focus

FIG. 76.



MILIARY TUBERCLES IN THE LUNG OF A CHILD. (*Birch Hirschfeld.*)

Thickened visceral pleura above. Three tubercular masses containing giant cells, caseous in the middle portions, non-vascular, surrounded by aerated vesicles with vessels in their septa.

the bacilli often cause capillary thrombi and new tubercles develop from these. Imperfect vascular supply is constant in tubercles. Beside distribution through the vessels, often after the wall of a vein is attacked, the lymph stream is commonly involved and ad-

CHAPTER XI.

METHODS.

A. Post-Mortem Examination.

A **CADAVER** is examined for the purpose of determining the cause and manner of death, but most often what we find is a series of anatomical changes in the organs, which we must then interpret, giving to each its relative value and deciding as well as may be which of several diseases probably determined death. If the case is one of legal importance the body should be identified, all distinguishing marks, scars, moles and deformities noted, with the weight, color of eyes and hair, number of teeth present and any gold or other fillings, and especially any external signs of violence. It is important here to distinguish injuries happening before death and those which may have occurred afterward; the main difference is that the ante-mortem wound presents evidence of bleeding, gapes if incised or torn, with beginning efforts at repair or evidence of inflammation, while post-mortem blows (later than two hours after death) do not usually produce ecchymosis, nor will incisions be followed by bleeding, and inflammatory and reparative changes are absent; microscopical examination may be required to decide the question. The first stages of decay often simulate ante-mortem lesions and must be recognized and separated from effects of disease (see pp. 94-95).

The post-mortem examination is divided into inspection of the exterior, section and examination of the various organs in a regular order and the summing up or gross anatomical diagnosis, to be followed by microscopical examination of the chief organs after hardening and section. The clinical history of the case

should always be read before beginning the autopsy, and the findings of the latter kept with a copy of the former. As the autopsy progresses the findings in each organ, with its weight, should be dictated to a scribe, and the whole signed by the pathologist, the microscopic examination added later.

External Inspection.

Weight of body; height measured between uprights as the body lies on the back; distinguishing marks, teeth, and wax cast of mouth if necessary; presence of decomposition as greenish hue of abdomen and prominence of superficial veins from imbibition of blood coloring matter; evidence of fractures, etc.; venereal scars and warts; presence of edema of ankles, scrotum, labia, ascites; post-mortem lividity, rigor mortis; skin lesions, tattoo marks; probable age of individual. If only part of a body is present, as head and upper extremities, twice the length of the arm, from the mid-sternal line to the tip of the middle finger (measured along the flexor surface in abduction), or the distance between the tips of the middle fingers along the flexor surface, the arms extended at right angles to the main axis; or, if but one extremity be present, the length measured from the glenoid cavity plus the distance between the glenoids, measured between perpendicular lines, or nineteen times the length of the middle finger will give the approximate height. The distance from the tip of the olecranon to the tip of the middle finger is about five-nineteenths of the height. The upper border of the symphysis in the adult is said to mark the mid-point of adult height, but this is not trustworthy, especially for women. From the head of the femur to the plantar surface of the heel is half the height, and the length of the femur alone is one-quarter of it. As many of these measurements as possible should be taken when necessary. Such estimates of the height and size of the total body may be of vast medico-legal importance (see tables of weights and measures, p. 308).

Internal Inspection.

Head and Brain.—Make incision from tip of one mastoid process over vertex to the tip of the other; if the body is bald carry the top of the incision a little farther backward; in any case cut through to the bone, strip up periosteum and scalp either side of the cut till two flaps are formed, reflect one over the face and the other backward; leave the temporal muscles for sewing, but cut through them with a knife where the saw cut is to come; begin the saw cut with the saw at right angles to the main axis of the skull at a point 3 cm. above the glabella, steady the blade against the thumb on the other hand, *pull* the saw till a good mark is made, cut with the thrust on a horizontal circumference on one side to 5 cm. above the mastoid tip, repeat on the other side, taking care not to go through dura; by a posterior saw cut running from one end to the other of the former line and about 3 cm. above the external occipital protuberance, complete the separation of the skull; the bone is thick at four points, in the mid line front and back and over either mastoid; at other points it is thin, especially in the temporal fossæ; a gentle blow with a chisel at one or more of these points may be needed. Then insert the blade of a strong forceps in the mid anterior cut and twist, then the jaws of the forceps and pull off the calvaria; if the dura is too adherent it may be taken along, or separated from the bone by a long blunt instrument. If dura and bone be not removed together, cut the membrane carefully from within outward along the saw cut; run a slender knife along the process to the crista galli and cut transversely, putting the dura on tension; strip it back from the vertex with slight touches of the knife over the parietal bodies. Note its blood content, presence of inflammatory exudates or blood on either surface, tumors, etc., slit up the superior longitudinal sinus and note the clot.

The pia is now exposed—note the blood content, presence of edema below or in its meshes, thickenings, pus, tubercles.

Gently lift up the frontal lobes and elevate the first nerves, cut through the optic chiasm, then the internal carotid of each side, always repeating on one side the incision done on the other and *using little force* ; run the knife, from below and within, out and back along the petrosal ridge, cutting the tentorium ; then divide the other nerves in order ; then the vertebral arteries from behind forward and as low as possible ; reach the scalpel with the blade forward down by the side of the medulla, rest the handle on the basal process as a fulcrum, turn the blade transversely, carry the handle toward the forehead which carries the blade back, cut the medulla as low as possible with a single clean sweep, drop the knife, support the vertex with one hand covered with a towel, reach in two fingers either side of the medulla and with a rotating motion about a transverse horizontal axis lift the cerebellar lobes out and up. Lay the brain on its vertex on a towel or in a pan of water and examine the base ; note the arteries, size, malformations, presence of atheroma, tubercles, follow them into the Sylvian fissures where sometimes tubercles are found when absent elsewhere and emboli and hemorrhage are common. Turn the brain on its base, separate the hemispheres, cut into a lateral ventricle along a line starting in the gray matter just anterior to the corpus callosum, running through the outer margin of the corpus backward into the convolutions over the posterior horn of the ventricle, the knife held at 45 degrees in the first third of the cut, more nearly horizontal in the middle third, and at 45 degrees in the last third ; the roof of the ventricle is usually opened in the mid-third posteriorly and may be completely opened by cutting from within out into each horn ; repeat on the other side. Lift up the anterior portion of the corpus callosum and dissect it backward off the velum and choroid plexus, cutting through the foramen of Monro upward, and behind sever one of the posterior limbs of the fornix and reflect to the side. With the pons and medulla supported on two fingers, cut through the vermiform process into the fourth ventricle, continue into the aqueduct and

the entire ventricular system is exposed. Make a series of antero-posterior wedges through each hemisphere, just external to the ganglia at the base, the thin edges of these coinciding; or make a cut just outside of the great ganglia from before backward to the pia, open the cut surface outward and make another at right angles to the first, another at right angles to this, always unfolding, and another; or make a series of sections of the entire brain running transversely across the main axis from above downward and before backward, better after hardening in Müller's fluid. The cerebellum is opened along the tree and by a series of cuts at right angles through each half. Lastly a series of transverse cuts through the ganglia, supporting them from below. The brain is then folded together again, turned over, and the pons and medulla sectioned transversely while supported by a finger or two below, the cuts placed close together. This method, though the one usually seen at necropsies, is essentially crude and many of the relations of different parts entirely destroyed; for fine work the entire brain should be hardened in alcohol or Müller's fluid or formalin solution before cutting. All cuts above given should go to the pia but not include it, and should be made with one firm stroke, the knife acting like a microtome knife and wet with water between each two sections; then no matter how much the original appearance of the organ is changed by the process, it may be restored by folding together and lesions localized by referring them to the chief fissures and convolutions, because the wedges of brain tissue are held together by the pia.

After examining the brain, break through the roof of the middle ear and of the orbits and examine the contents of each; if the eye is wanted for further examination, it may be cut just behind the conjunctival margin and removed, the anterior half left in situ and stuffed slightly with cotton. Some of the great ganglia of the skull are easy of access, especially the Gasserian, lying on the point of the petrous bone just under the dura mater.

If fractures have been found in the skull the dura should be stripped from the base and the lines of fracture traced before the ear and eye cavities are opened, and chisel and mallet must not be used till the injuries are fully described ; in medico-legal cases, not at all.

The spinal cord may be removed either before or after the thorax and abdomen are examined. The body is laid prone, the head hanging over the edge of the table, the abdomen laid on a block of wood to lessen the lumbar curve. An incision is made along the spinous processes and integument and muscle removed to one side from the lateral spinal groove ; repeat on the other side ; see that the bottom of the groove is clean, exposing the laminæ, saw through these so as to enter the outer part of the canal but not to injure the cord (about 1 cm. from spinous processes) ; be sure to sever the laminæ completely with the first sawing ; strike the spinous processes on one side with a mallet and then on the other and cutting through the ligaments in the lower lumbar region lift up the freed spines in one long series with a strong forceps. Pick up the dura over the cauda equina with a pair of mouse-toothed forceps and cut the nerves from below upward one side and the other, and with a little care most of the posterior root ganglia can be removed with the cord ; do not handle the cord with any force or allow it to be bent. Lay it on either its front or posterior side and open the dura carefully with a probe-pointed scissors. With a sharp razor make exact transverse cuts through the cord between each two pairs of nerves leaving the segments attached by pia ; hang the cord in a tall jar of Müller's fluid with a light weight at the lower end till hard enough to cut. Examine the vertebræ for dislocations, etc. After the trunk viscera have been removed the spinal canal may be opened from the anterior aspect by means of a strong curved chisel, but the results are not so satisfactory as by the other method.

Thorax and Abdomen.—Body on its back, long single incision from 3 cm. above episternal notch to pubes, going to the left of the

umbilicus, the knife held in the whole hand with the wrist firm, the movement taking place chiefly at the shoulder joint. *Do not make any cuts with the index finger on the back of the knife!* As the first cut opens the abdomen, usually in the upper zone, a finger may be hooked into the cut and the abdominal wall lifted strongly toward the operator and the incision completed, the knife inserted external to the peritoneum just over the pubes and the tendon of the rectus abdominis severed. Then hook the thumb under the abdominal flap nearest, spread the fingers on the thorax, press with fingers and pull with thumb to make the free edge of the costal cartilages prominent, and cut along their margin; grasp the integument and muscles over the thorax firmly, pull strongly toward you, and sweep the thoracic wall clean with long cuts of the entire blade; repeat on the other side. Lay the knife down and inspect the abdomen, *not touching anything, merely looking*; note the position of the organs, presence of fluid and character, and catch what runs off for measurement; then lift up the omentum and examine the coils of intestine. The normal peritoneum is shiny, like all serous membranes, and transparent. With the palm upward reach under the ribs and determine the height of the diaphragm on each side in the mid-clavicular line, usually about the fourth rib or space on the right side, and a rib or space lower on the left; if unusually low it points to fluid or increased volume of organs in the thorax. If pneumothorax is suspected, hold the skin and muscle flap of the thorax up and fill the groove next the ribs with water, puncture a space below the level of the water and note bubbles issuing from thorax. Or water may be put in the upper abdomen and the diaphragm punctured. Now cut the costal cartilages from the second down, sweeping lightly outward to the ninth, resting the knife on the following one of each pair before the former is quite cut through, holding the knife as horizontal as possible, to avoid cutting the lung. Lift the sternum by the xiphoid cartilage, transfix the attachment of diaphragm so that the knife comes out in the line of section of the cartilages and cut away from the xiphoid and out, repeat on the

other side ; now grasping the end of the cut cartilages on one side lift the sternum strongly upward and dissect it from the thoracic contents by long transverse sweeps of the knife, keeping close to the bone to avoid opening the pericardium ; when this is complete as far as the first rib the knife should be carried out toward the shoulder about 4–6 cm. and the cartilage cut upward on each side. Disarticulate the clavicle by running a slender knife along the line of the joint, entering it from the episternal notch, curving down and out, holding the handle of the knife nearer the subject's chin than the blade because the plane of the joint slants and a perpendicular knife meets sternum above and clavicle below ; this is often one of the hardest points for a beginner in making autopsies, but if the plane of the joint be kept in mind and the knife slanted properly it follows the joint without the need of any great force. The sternum being practically freed from all its attachments should be *twisted out* rather than cut, to avoid escape of blood from the large veins of the neck into the thorax.

The lungs and heart are exposed ; note how nearly the former approach in the median line, normally they touch at the second rib. Note adhesions in the thorax, measure fluid. Open the pericardium by picking up a fold and incising transversely ; air rushes in and the point of the knife is then carried down to the apex, up to the base, and over to the right from about the middle of the main cut, always from within out. Note the condition of the pericardium and its contents ; measure the latter if abundant. Feel the great vessels for aneurysm.

Grasp the heart by the base and turn it up to expose the posterior surface, estimate by the eye a line midway between the anterior and posterior coronary arteries and along this cut into the left ventricle from the base to the apex with one long sweep of the knife ; open the right ventricle by a similar cut midway between the posterior coronary and the right (really the inferior) margin of the heart, the space being usually quite free from fat ; as the left ventricle is opened insert the index finger of the left hand, put the thumb into the other cut—between the

two is the septum—and with that hold the heart is easily managed in the further cutting ; avoid pressing the septum between thumb and finger. Lift the organ straight up and cut the stretched vena cava inferior as long as possible just as it enters the pericardium ; swing the heart to the right side and cut the pulmonary veins on the other, reverse and cut the remaining pulmonary veins and superior cava ; only the aorta holds it now and that is cut from below upward as the heart is lifted and carried toward the chin ; if the knife is sharp and clean long cuts are made, two or three are enough and there is no spattering of blood. Lay the heart on its front ; having kept the original hold the inferior vena cava is above the thumb ; enter it with the probe end of the enterotome and come out the superior, and then with a single cut open the right auricle, turn out the clots ; reverse the scissors, enter the probe blade from above through the tricuspid valve and out of the first knife cut and thus open the ventricle ; on the anterior flap of the right ventricle, thus formed, look for a papillary muscle, pass the probe blade in front of this and cut on the anterior wall across to the pulmonary valve, aiming for a small pledget of fat on the infero-anterior aspect of the pulmonary conus and thus cutting into the artery between the cusps of the valve. Open the left auricle by cutting from one pulmonary vein to another ; run the probe blade from above through the mitral and bring it out of the first cut, thus cutting through the external flap of the mitral. Now turn the apex of the heart toward you, pass the probe blade behind the internal flap of the mitral and on the anterior surface cut from apex along coronary artery *but not across it* to the appendix auriculæ ; stop cutting and push the probe blade out of the aorta, rotate the hand outward (supinate) about fifteen degrees and cut into the aorta, drawing the pulmonary artery out of the way with the left hand. Thus the entire inner surface of the heart with its four valves is exposed by two cuts in each auricle and two in each ventricle, of which latter the first is made on the posterior surface of the ventricle

before the heart is taken out, and the second on the anterior surface after removal. Wash out clots, weigh the heart, measure its walls, estimate the capacity of each chamber, note the condition of the valves and the muscles, examine the arch of the aorta for atheroma, slit up one or both coronaries.

The competency of the cardiac valves can be better determined by careful inspection than by passing two or more fingers into them while uncut and estimating their size by the degree of separation possible between the fingers, and so-called hydrostatic tests are equally untrustworthy.

The lungs may be removed by grasping each firmly by the apex, drawing it horizontally toward the symphysis, thus making the structures at its root tense, and cutting across them, or by lifting one out of the chest till it rests on the ribs and then cutting across the bronchi and vessels. Usually both are removed before either is studied; they can be referred to the proper side by remembering that the posterior border of each is rounded, the anterior margin thin, the base a shallow cup to correspond with the diaphragm, and the bronchi, etc., on the inner aspect; set the organ on its base, the apex is at once evident and the borders determine its relation in the body; the right lung has three lobes normally and the left but two, but variations are common. Note the condition of the pleura; if firm old adhesions are present it may be necessary to make an incision in the costal pleura and strip it from the inner side of the ribs, removing both layers with the lung. Open the large bronchi with a probe-pointed scissors, and the vessels likewise. Lay the lung on its inner surface and make a single long cut through its rounded posterior margin from apex to base and from pleura to hilum. The object of such long smooth cuts is to secure a smooth even surface for inspection, and they require and repay careful practice. Note the relative air and blood contents of the lung, its solidity, color, smoothness of section, density and friability on gentle pressure with the finger; cut off a shaving from the most solid part and see if it floats in water. Weigh each lung.

With the enterotome cut the diaphragm on each side of the middle line back to the spine and rotate the liver upward into the thorax, to gain more space for the abdominal organs.

Remove the spleen by gently drawing it toward the middle line and cutting from above downward across its hilum on the external aspect. Note its size, weight, conformation, condition of capsule, presence of infarcts ; make a single long cut through it and note the lymphoid elements, proportion of fibrous tissue, consistency of the organ as a whole ; if waxy, test for amyloid changes.

The omentum may be removed after inspection when first reflected after the abdomen is opened or at a later stage. It is well now to lift up the small intestine near the cecum, cut through the mesentery and then gently pulling on the gut with one hand, keep drawing a sharp knife across the mesentery like a violin bow, close to the gut, cutting only mesentery but doing that thoroughly, keeping the knife nearly flat, putting the intestine into a special pan as taken out ; cutting thus from below upward, when the duodenum is reached it is ligated and cut distal to the ligature. The stump of the mesentery is then removed. The large intestine is removed by drawing the cecum toward the middle line, cutting the peritoneum externally, lifting the gut up and toward the opposite side and dissecting it off subjacent structures, being careful not to wound either the right kidney or the duodenum ; it is then separated along the transverse portion from the stomach and from the splenic flexure downward to the rectum, which is tied and cut ; or, more conveniently often, from rectum to splenic flexure as on the right side, from below up. The entire gut is now opened separately in the sink, washed and studied, the small intestine being cut along the mesenteric attachment and, if necessary, the contents of each portion is caught in a separate basin for further examination.

The kidneys are now removed with the adrenals, either by making a superficial cut across the hilum of the organ through the peritoneum, inserting two fingers of each hand and shelling

the organ out of its fatty capsule, or by cutting on the outer aspect, drawing the organ across the spinal column and taking the fatty capsule with it; in either case it is well to cut the vessels from above downward and when free from them, by gently pulling to disclose and examine the upper portion of the ureter; if necessary the urinary tract may be removed entire and in that case the ureters are dissected down to the bladder, and with the attached kidneys turned downward till the pelvic organs are removed. Each kidney should be freed from its proper capsule by a very superficial incision through it along the convexity of the organ which permits it to be stripped off, the inner side of the capsule examined, as also the surface of the organ, to see if kidney tissue is torn off with the capsule. The color, blood content and smoothness of the kidney surface are noted and cysts and infarcts described. A long incision is made through the convexity of the organ down to the pelvis, opening it; the capsule and fatty tissue tucked between the middle and ring fingers of the left hand allow complete control of the organ while this cut is being made. The relative proportion between cortex and medulla is noted, color of cut surface, presence of fat and urinary salts in the tubes, prominence of the glomeruli in active hyperemia, increase of connective tissue, state of the pelvic mucous membrane, capacity of the same, etc.; weight of kidneys. If waxy test for amyloid.

The liver is grasped by the left hand, the fingers behind and over the convexity, the thumb in the anterior notch, and the organ thus firmly held is lifted while its attachments are cut, the knife laid aside for a moment while the portal vein and common bile duct are palpated. Without changing the hold described the organ is lifted and freed, then weighed, and examined externally; one or several long anterior cuts across both right and left lobes are made and the blood content, amount of connective tissue, bile staining and presence of fat determined. If waxy test for amyloid.

The ligatured end of the duodenum is now lifted and it is re-

moved from below upward with stomach and pancreas. The stomach is opened from above along its greater curvature and into the duodenum, its contents caught in a clean pan for examination, the condition of the mucous membrane noted. The stomach may also be opened the first thing after the thoracic organs, by slitting the upper third of the duodenum and cutting along the greater curvature ; gentle pressure along the course of the common bile duct causes bile to exude, or, if not, a probe can be inserted as far as it will go and the duct traced out while the relations of the liver are unchanged. A series of transverse cuts along the entire length of the pancreas is made and the cut sections examined ; small points of fat necrosis should be looked for, and the pancreatic duct opened and traced.

When the organs in the neck are examined the knife is swept within the ring of the two clavicles close to the bone, the tissues under the skin on the front of the neck dissected free as far as the hyoid body and from here to the symphysis ; the knife is then pushed through the floor of the mouth directly behind the symphysis and swept back and out close to the inner surface of the lower jaw as far as the angle, and from here back and in to the vertebral column. Then the trachea and esophagus are elevated toward the chin and the dissection carried up behind them as far as opposite the roof of the mouth ; the tongue is then drawn downward, the lateral pillars of the fauces and the soft palate severed and the entire group of structures removed. The esophagus is opened on its posterior aspect from the pharynx down, then pulled to one side while the trachea and posterior wall of the larynx are opened with scissors.

The pelvic organs are removed together by cutting through the peritoneum along the brim of the pelvis and by blunt dissection separating it from the inner pelvic aspect as far as possible. Then the cut and tied end of the rectum is grasped and pulled strongly up and toward the symphysis pubis while dissection is carried on behind it. The pelvic contents are now attached only around the margins of orifices leading out of the cavity, and

by traction on rectum and bladder together these attachments are made tense and cut across.

The rectum is then opened on its posterior aspect and examined. A notch is made in the vertex of the bladder with the enterotome and the cut made on the anterior wall, the probe-point passing out of the meatus internus. The uterus may be opened on either the anterior or the posterior surface, preferably the latter, by a sharp knife, just cutting into the cavity; section into the vagina is completed with scissors *from above downward*; in this way the pathologist knows that if anything is found in the uterus he did not carry it up from the vagina on the point of his scissors, a matter of importance in medico-legal inquiries. Secondary cuts open the cornua and display the entrance of the tubes. A single long cut in each ovary is usually enough; the testicle may be pushed up to the internal ring and there cut into without mutilation of the external genitals.

In many cases it is desirable now to slit the vena cava inferior and abdominal and thoracic aorta from below upward, and to cut out a portion of a rib and also of one of the long bones.

The calvaria is replaced and held by two stitches in the halves of the temporal muscle and the cut in the scalp, as well as the long cut from episternal notch to pubes, closed with waxed white cord in a glover's suture.

Ordinarily a post-mortem examination made as given is adequate for the case studied, or all that is allowed by the friends; the order in which the organs are examined is the usual one and convenient in most cases, but often it is necessary to vary it. In medico-legal inquiries it is of the utmost importance to make a complete and accurate record, with measurements and weights, a photograph of the body and of important injuries, chemical examination of stomach and intestinal contents, and careful distinction between what was pathological in the various organs, what was due merely to post-mortem decomposition and what the pathologist was obliged to do in order to examine the parts.

The following may be taken as a fair sample of an autopsy

record in ordinary routine hospital work and no less than this should ever be included in the pathologist's report.

RECORD OF AN AUTOPSY ON THE BODY OF

John ———, aged 35, German, married, carpenter. Residence or hospital ward ———.

Died January 1, 1901, 11:30 P. M.

Autopsy January 2, 1901, 2:00 P. M.

Clinical diagnosis—pyemia.

Inspection.—Body well nourished, height five feet seven inches, rigor mortis well marked in lower extremities, absent in arms, blue anchor tattooed on left forearm. Incised wound on left leg, upper third, external aspect, 12 cm. long, edges everted and colored green to black, surface partly granulating and partly covered with thin pus and necrotic tissue, odor foul. Abscess cavity in left groin about as large as a hen's egg, apparently opened by incision, no evidence of healing. Tissues of left thigh edematous. Right knee swollen and distended with pus.

Peritoneal Cavity.—Small collection of pus localized between spleen and ribs, communicating with small abscess cavity in spleen, shut off from general peritoneum by recent adhesions.

Diaphragm.—Right side fifth rib, left side fifth space.

Thorax.—Small amount of turbid serum in right pleural cavity, no adhesions either side.

Pericardium normal. Heart weighs 360 grams., muscular tissue pale and soft, valves competent, small recent vegetations on mitral and aortic valves with subendocardial hemorrhages in the neighborhood, vegetations on ventricular aspect of each valve, easily detached.

Right lung presents an area of red hepatization on posterior third of lower lobe, remaining portions congested and edematous, bronchial mucous membrane congested and covered with muco-pus.

Left lung contains several small foci of pus in both lobes, the largest about the size of a hazel nut, with a zone of red hepa-

tization about each ; dependent portions congested, whole lung edematous. A small area of caseous material in the apex walled about with firm fibrous tissue. Bronchi as above.

Abdomen.—*Spleen* large, soft, weighs 340 grams, presents an abscess cavity on outer aspect which communicates with a collection of pus as described above. The rest of the organ very congested.

Kidneys, weight together 375 grams. In each the capsule is not adherent, surface smooth with dark mottlings, cortex swollen, its markings very indistinct, pyramids darker in color, pelvic membrane normal.

Intestines.—Small intestine normal ; large intestine shows some edema of mucous membrane, solitary follicles prominent and here and there ulcerated and surrounded by zones of hyperemia.

Liver.—Weight 2,560 grams, the acini contain much fat in their peripheries. Gall-bladder contains one small calculus ; bile normal.

Pancreas apparently normal.

Pelvic organs normal.

Head. *Brain.*—*Dura* normal. In the meshes of the pia over the vertex, between the convolutions and at the base, especially along the Sylvian fissure, there is pus in appreciable quantities.

Spinal cord not examined.

Veins.—Partly softened thromboses in left external iliac vein just above Poupart's ligament, loosely attached to the vein wall, about 5 cm. long, color reddish.

Gross anatomical diagnosis ; pyemia, malignant endocarditis, meningitis.

A——— B———, M. D.

Space for histological and bacteriological report.

B. Disposition of Material ; Preservation ; Hardening.

Fresh material gathered at the autopsy may be immediately cut by the freezing microtome and the sections examined, but

as a rule all tissue has to be put through various processes to fit it for microscopical study. The tissue elements must be fixed in the position and condition sustained during life, hence it is important to gather material in as fresh a state as possible, and they must also be hardened to resist the various stains and dehydrating fluids with which they are treated later. Often the same fluid accomplishes both results, fixing the cells, hardening the tissues and also producing optical differences, which aid further study, and as a rule the best fixatives are mixtures with an acid reaction; they vary much in power to penetrate tissue and hence for some fluids the material must be cut into small pieces and exposed to a great bulk of fixative. Heating the material in the fluid increases penetration. After fixing, the tissue must be thoroughly washed to remove the fixative, or staining will be imperfect; tissues hardened in bichloride of mercury, chromic acid and chromate solutions may be washed out with water; picric acid and its compounds require alcohol and heat facilitates the process.

Fresh Material. *Fluids.*—Put a drop on a slide, cover quickly and examine with a half inch and then with a sixth; if rich in cells, thin with normal salt solution (0.6 of one per cent.). A little vaseline along the cover-glass will prevent too rapid drying. If the fluid is poor in cells, sediment in the centrifuge. If desired to keep the fluid for a time, make a hanging drop over a hollow slide and ring with vaseline. Tissues may be scraped over a smooth cut surface and the material so obtained examined as above. A little of such fluid may be taken on the end of a slide and drawn smoothly over another and the film on the second slide studied before or after drying and staining. Elements may be fixed on the slide by coating it first with white of egg and glycerine, or by gentle heat over a Bunsen burner after the spread is dried in the air.

Tissues often require to be thoroughly teased in normal salt solution, glycerin, hydrocele or ascites fluid, and sometimes it is well to soften the tissue first to loosen the attachment of

cells to basement substance ; this is called maceration and the fluids most used for the purpose are :

1. Alcohol, 33 per cent. (Ranvier's). Soak the tissue 24 hours in small pieces ; good for muscle and gland tissue.
2. Freshly made potassium hydrate solution, up to 32 per cent., which is very rapid, 10 to 15 minutes ; tease in the solution, not in water ; to preserve the specimen, take it from the potassium solution and put it into 50 per cent. acetic acid, wash thoroughly, then wash in water, mount in glycerin after staining with alum carmine. Good for smooth muscle and tissues containing it.
3. Chromic acid and its salts (acid 1 to 20,000 ; Müller's fluid or 2 per cent. potassium bichromate) leave in the former 24 hours, in the latter 2 to 5 days ; good for nervous tissue, ganglion cells, etc.
4. Osmic acid, 1 per cent. solution, for nerves.

To clear up certain details it is well to treat fresh material with various chemical fluids, and they may be allowed to flow under the cover-glass if a drop is put on one side and a small piece of blotting paper on the other :

1. Acetic acid swells connective tissue and cell protoplasm and renders them transparent, shrivels nuclei and makes them prominent, precipitates mucin, distinguishes between fatty and albuminous granules by promptly dissolving the latter, elastic elements and parasites not influenced and hence allowed to become prominent ; may be used pure (glacial acetic) or in various dilutions, 2 to 5 per cent. best.

2. Potassium acetate, saturated solution in water ; clears, and makes nuclei prominent.
3. Potassium and sodium hydrate solutions, 1 to 3 per cent., dissolve most tissues, leave elastic, fat, pigment, amyloid, bone and bacteria untouched. Macerate if strong.
4. Hydrochloric acid, 3 to 5 per cent. dissolves osseous tissue with production of CO_2 bubbles. Dilute sulphuric acid also dissolves bone and crystals of calcium sulphate form.
5. Osmic acid, 1 to 2 per cent., colors fat black.
6. Dilute iodine solution, best in the following :

Iodine,	1.0
Potassium iodide,	1.0
Distilled water,	100.0

Mix ; dilute with 3 to 5 parts water for use ; this renders nuclei and cell contours distinct and colors glycogen and amyloid brown.

7. Staining solutions of various kinds may be drifted under the cover-glass in the same way and the excess washed out with distilled water.

Fixation and Hardening.

General rules—

Cut the tissue into cubes not larger than 1 cm. on each edge.

Use 10–20 times as much fluid, bulk for bulk, and change if it grows turbid.

Put a layer of absorbent cotton or filter paper in the bottom of the jar, that the fluid may act from all sides and discoloration by precipitates be avoided.

After the tissue is hard enough, wash 12-24 hours in running or frequently changed water and then put into graded alcohols, 70, 80 and 90 per cent., each for 24 hours.

Usual fluids for this purpose are :

I. Alcohol.

Ninety per cent. to absolute alcohol, changed every 6-8 hours for three times; preserve in 90-95 per cent. Good for rapid work and where bacteria are suspected in the tissue; also, if substances present, as glycogen, which are soluble in water. After preliminary hardening by other methods, graded alcohols are used, beginning with 70 per cent. This method is not so much used as formerly, because of the shrinking in the preparation and destruction of red cells and pigments. Ordinary "absolute" alcohol of commerce is seldom more than 95 per cent.; to remove the remaining water, heat copper sulphate crystals till the water of crystallization is driven off and most of the color is lost, pulverize and add this in at least the proportion of one-third to the alcohol bottle; repeat the process when the copper salt begins to turn blue; filter the alcohol before use.

II. Formalin.

To an increasing extent this agent has taken the place of alcohol, being satisfactory for both animal and vegetable tissues and preserving the natural color more than alcohol. Formalin of commerce is a solution of formaldehyd in water, about 40 per cent., and the usual dilution used for hardening is 5 per cent. for 12-24 hours, 2 per cent. for two or three days, or, for rapid work, as high as 50 per cent., for half an hour to an hour. The weak solution is usually to be preferred, as with stronger a precipitate may occur wherever there are red blood cells. It preserves these cells intact, stops the further development of bacteria at once, penetrates well, causes no shrinking and does not injure the tissue if left for a long time. Combinations with

other fluids are often valuable, as Orth's mixture of Müller's fluid with 10 per cent. formalin, usually made fresh, good for about four days after making, hardens in 3 to 12 hours; wash well in running water afterward. Formalin may be kept in dark glass bottles, as paraform is apt to precipitate under the influence of light; if this happens a small addition of water and heating redissolve it. Strong formalin is irritating to eyes and hands.

III. Corrosive Sublimate Solution.

This has so little penetrating power that the pieces of tissue must be very thin and shrinking may occur, but it fixes cells and karyokinetic figures and preserves red cells and pigment. It is used as

1. Concentrated aqueous solution, 3-6 hours.
2. Normal salt solution saturated with bichloride by the aid of heat (about 7 per cent.); 3-6 hours.
3. Acetic sublimate solution:

Glacial acetic acid,	1 part.
Corrosive sublimate,	3 parts.
Distilled water,	100 "

Leave tissue about twenty-four hours; does not shrivel.

4. Zenker's fluid:

Sodium sulphate,	1.0
Potassium bichromate,	2.5
Corrosive sublimate,	5.0
Distilled water,	100.0

Make solution by the aid of heat; just before using add

Glacial acetic acid,	5.0
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Use about 24 hours; as after all the others, wash thoroughly in water and carry through graded alcohols.

IV. Chromic Acid and Solutions.

Solutions in water of 0.05–0.5 per cent. for 24 hours to several days, changed daily, penetrates slowly, makes staining uncertain; hence almost discarded for chromate salts. Harden afterward with alcohols in the dark.

1. Müller's fluid :

Potassium bichromate,	2.5
Sodium sulphate,	1.0
Distilled water,	100.0

Use in large amounts with daily changes for the first week, then every two or three days, then every week, for ten weeks; add a small lump of camphor to prevent formation of mold. The process may be shortened by setting the preparation in the thermostat at 37°–39° C., changing the fluid daily; two weeks enough. Tissues when hard may be cut at once by the freezing microtome or carried through alcohols and embedded; they must be well washed in water and hardened in alcohol in the dark. The sections stain well with hematoxylin-eosin and some carmin stains. Müller's fluid preserves red cells and gives a good section with paraffin in imbedding, but it does not stop the action of bacteria in the tissues for some time, injures nuclear structure, and stains the tissue dark yellow. For nervous tissue a mixture with formalin is advisable, as

2. Commercial formalin,	10.0
Müller's fluid,	100.0

After a time the tissue becomes brittle in this mixture. Formalin may be used alone first and then the Müller's fluid.

3. Erlicki's fluid :

Potassium bichromate,	2.5
Copper sulphate,	0.5
Distilled water,	100.0

Hardens in 8-10 days, but the tissue often shows precipitates.

V. Osmic Acid and Mixtures.

Make always with freshly distilled water and keep in glass-stoppered bottles in the dark ; use small pieces of tissue (1-2 mm. thick) and stir them frequently ; fix in the dark, especially with osmic acid ; wash well afterward ; imbed in paraffin, not in celloidin, because ether dissolves out the fat stained black by the acid, and use chloroform or clove oil, xylol also dissolves the fat ; clear with ethereal oil ; mount in thick Canada balsam containing as little xylol as possible, softening it by heat.

1. Pure osmic acid, 1 per cent. solution, after 24 hours wash and harden in alcohol, stain with safranin or toluidin blue.

2. Fleming's mixture :

1 per cent. chromic acid,	15 parts.
2 per cent. osmic acid,	4 "
Glacial acetic acid,	$\frac{1}{2}$ -1 part.

Tissue left 24 hours, well washed, hardened in graded alcohols ; good for karyokinetic figures and structure in general ; sections take carbolic fuchsin, gentian violet and safranin well, hematoxylin not so well.

3. Hermann's mixture :

1 per cent. platinum chloride, 15 parts.
2 per cent. osmic acid, 4 "
Glacial acetic acid, 1 part.

Thin pieces from 1-4 days, wash 3-12 hours, harden in alcohols ; stain with safranin or gentian, good for nuclear and also protoplasmic structure.

4. Altmann's mixture :

Potassium bichromate sol., 5 per cent.
Osmic acid, 2 " "

Mix in equal volumes, leave tissue (*taken immediately after death and cut very thin*) 24 hours, wash well, harden in alcohols, imbed in paraffin.

VI. Cooking.

Small cubes of tissue may be dropped into boiling water for $\frac{1}{2}$ to 1 minute and then carried through graded alcohols ; good for edema, especially pulmonary, albuminous exudates, as in kidney, etc.

Decalcification.

General rules :

Use plenty of fluid ; small pieces of tissue, wash thoroughly afterward ; in the case of some methods fix well first (see below) ; imbed in celloidin usually ; the tissue is pliable when decalcified and allows a needle to penetrate it easily.

1. In Müller's fluid : Fix in formalin, leave small pieces several months to a year with daily changes at first ; or hasten the process in the thermostat ; good for bones of fetus and infant.

2. In picric acid : Fixing not necessary ; use saturated aqueous solution several months ; good for small bones, but very slow ; to remove the picric acid, wash and lay in alcohol to which twenty to thirty drops of saturated aqueous solution of lithium carbonate have been added, more lithium will be required from time to time till the tissue is pale in color.

3. In hydrochloric acid : Used alone in 3-5 per cent. solution, but injures the tissues and the following are better :

4. Ebner's fluid, aqueous :

Sodium chloride sol., saturated,	100.0
Distilled water,	100.0
Hydrochloric acid,	4.0

Leave the fixed and hardened osseous tissue till decalcified, adding 1-2 cc. HCl every day or so ; wash and put through alcohols.

5. Ebner's fluid, alcoholic :

Hydrochloric acid,	2.5 to 5.0 to 10.0
Alcohol,	500.0
Distilled water,	100.0
Sodium chloride,	2.5 to 5.0

Fix beforehand ; the more powerful solution hastens the process, which is slow at best.

6. In nitric acid : Thoma's method. Fix and harden ; put the tissue in

Alcohol,	5 parts.
Nitric acid,	1 part.

for two or three weeks ; change the fluid frequently ; wash in alcohol ; remove the acid thoroughly by alcohol to which has been added calcium carbonate in excess.

7. Phloroglucin : Make a stock solution as follows :

Nitric acid, C. P.,	10 cc.
Phloroglucin,	1 gm.

Dissolve carefully ; if with the aid of heat, under a hood ; then add

Distilled water,	50.0 cc.
for use add	
Nitric acid,	10.0 cc.
Distilled water,	50.0 cc.

This acts very rapidly, 30 minutes to 12 hours according to age and size of bone ; wash in water 48 hours.

8. Trichloroacetic acid : Tissue fixed, put in 5 per cent. aqueous solution of the acid, often changed, ready in 5-6 days ; results very good usually.

Injection.—Lumina, especially of blood-vessels, are often filled with some injecting material. This usually consists of a vehicle and a dye, but the method is seldom required for pathological work and hence but two or three of the common fluids need be mentioned. The most important vehicles contain either glycerin or gelatin ; the latter require to be heated, the former may be used cold. To avoid the need of heating gelatin a solution is made and heated for several hours with the addition of a little ammonia ; this when cool does not become solid, but after injecting (a dye being added) the preparation may be put into strong alcohol or dilute chromic acid and the mass sets.

Cold Injection Fluids.

Richardson's blue :

Solution No. 1.	{ Sulphate of iron,	0.62
	{ Distilled water,	30.0

Solution No. 2.	{	Red potassium ferrocyanide,	2.0
		Distilled water,	30.0
Solution No. 3.	{	Distilled water,	60.0
		Glycerin,	30.0
		Alcohol,	30.0

Slowly mix 1 and 2, shaking ; to the greenish blue opalescent fluid add 3 gradually, shaking.

Beale's Prussian blue :

Glycerin,	32.0
Alcohol, 50 per cent.,	32.0
Potassium ferrocyanide,	0.75
Tincture of perchloride of iron,	4.0
Distilled water,	128.0

To one-quarter of the water and glycerin add the ferrocyanide, to another add the perchloride, add *the former to the latter* very gradually and shake in a bottle ; add the alcohol and the rest of the water slowly with constant shaking. Preserve specimens in glycerin with 1 per cent. acetic acid.

Warm Injection Fluids.

Robin's gelatin vehicle :

Gelatin,	1 part.
Cold water,	7-10 parts.

Soak for a while, then heat over a water-bath ; add 2 per cent. chloral hydrate to prevent mold ; add for use one of the dyes given below.

Robin's glycerin-gelatin vehicle :

Gelatin,	50.0
Water,	300.0

(in which a little arsenious acid has been dissolved)

Glycerin,	150.0
Carbolic acid,	0.50

Mix on a water-bath in the order given.

Beale's carmin mass :**No. 1 :**

Carmin,	32.0
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Moisten with a little water and complete solution by adding

Ammonia,	0.35
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add, shaking

Glycerin,	15.0
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No. 2 :

Glacial acetic acid,	0.50
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Glycerin,	15.0
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Add 2 to 1 shaking and dilute for use with

Glycerin,	15.0
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Alcohol,	7.5
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Distilled water,	22.5
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One part of this mixture is added to 3-4 of either vehicle given above. Such injection fluid is used warm and the object to be injected is kept in a large vessel of warm water till the operation is complete.

Prussian blue.**No. 1 :**

Potassium ferrocyanide, saturated

sol.,	90.0
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Glycerin,	50.0
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No. 2 :

Liquid perchloride of iron at 30°,	3.0
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Glycerin,	50.0
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Mix slowly, combine with 3 parts of vehicle, add a few drops of hydrochloric acid.

C. Imbedding and Sectioning.—Two methods are employed for imbedding pathological material, namely with paraffin and with celloidin, the latter being somewhat easier to manage than the former; both have for their purpose such impregnation of

the tissue spaces with an indifferent and easily sectioned substance that the microtome knife will make thin and even sections without tearing and the various elements will retain their relations. Paraffin is a good example of an imbedding mass which is used hot and becomes firm on cooling; celloidin works on the principle of solution in a volatile fluid with firm consistency after the same has evaporated, and as a general rule the latter is used for large objects and the paraffin for small. Paraffin is best where very fine work is done and thin sections necessary, and yet, as it is brittle, material over 1.5 cm. on the edge may not give a thin section or perhaps even a complete one; and hence the method chosen depends on experience and convenience and the size and nature of the tissue to be cut. Where it is desirable to use paraffin for large pieces of tissue, a paraffin with a low melting-point ("soft" paraffin) will serve.

Paraffin.—Tissue must be well freed from water by absolute alcohol; dehydration may be hastened by laying material in anilin oil a few hours (up to 10). Then in

Xylol, changing two or three times, for about three hours at the outside, to remove the alcohol. Next in

Xylol and paraffin (see below) for 2–3 hours, and the process may be hastened by heating on a water-bath or a paraffin stove to about 52° C. Then in—

Melted paraffin. Two grades of paraffin are all that are usually needed in laboratory work, one melting about 56° C. and the other about 45° C.; by combining these different proportions a mass may be obtained which will be suited to the temperature of the laboratory, using more hard for warm weather and more of the soft for cold. Thus 25 gm. hard with 30 gm. soft will give a mass whose melting-point is about 52° C., and will serve quite well for ordinary room temperature (up to 20° C.). By using a hot or a cold knife according to circumstances the same mixture will cut over a wide range of temperatures. The paraffin is melted on a water-bath or a special oven at a constant temperature; sometimes it cuts better after strongly overheating,

which is equivalent to raising its melting-point for the next time it requires more heat. A little of the melted paraffin is poured into a glass dish, which may be lightly wiped with clove oil or glycerin beforehand to prevent sticking; when nearly solid, the tissue is set in and more paraffin poured till the material is covered; the whole is then rapidly cooled by setting the dish a little way into cold water, or on a marble slab; rapid cooling prevents crystallization and brittleness; water must not touch the paraffin at any time during the process. Instead of glass dishes little cases and half tubes may be made of stiff paper, wrapped about blocks of wood, or a cork may be put into a short glass tube, paraffin poured on this, the tissue added, and the plug of paraffin and specimen thus formed pushed out when hard. The superfluous mass is pared off before cutting, paper removed, fastened to a block of hard wood or hard paraffin by the aid of heat, clamped in the microtome and cut, with the knife at right angles if the block is small, and somewhat slanted if larger; the former is apt to give a section smaller than the surface of the tissue, from squeezing and compression; the latter is apt to give a rolled or curved section. This may be controlled by lightly holding the section by a camel's hair brush as it is cut, or as in serial cutting. The steps of ordinary imbedding are then as follows:

1. Alcohol, absolute, to dehydrate (perhaps with anilin oil), 8 to 12 hours.
2. "Clearing," or impregnation with xylol, change 2 to 3 times, 2 to 3 hours.
3. Xylol and paraffin 2 to 3 hours.
4. Paraffin, melted; change once or twice; 2 to 5 hours.
5. Pour in mold and harden quickly.
6. Trim and fasten on block for cutting.

Rapid method for diagnosis of tissue scrapings, etc.

Tissue small and 1 to 3 mm. thin on blotting paper or cotton in absolute alcohol, $\frac{1}{2}$ to 1 hour, change once.

Then in closed glass vessel with anilin oil, and put in thermostat or paraffin stove at 50 to 55° C., $\frac{1}{2}$ to 1 hour.

Xylol changed 2 to 3 times, $\frac{1}{2}$ to 1 hour.

Paraffin, melted, once changed, $\frac{1}{2}$ to 1 hour.

Mold, pare and cut.

Several other fluids besides xylol can be used, as :

Turpentine, which may injure delicate tissues.

Clove oil penetrates well, mixes with paraffin badly.

Chloroform, mixes well, requires to be driven off completely by heat, penetrates slowly, hence reserved for small objects and those hardened in chromic and osmic acids.

Bergamot oil, good for delicate tissue and to prevent shrivelling, used in equal parts with alcohol for 2 hours, then pure, then the soft paraffin, and lastly the mixture given above.

Anilin oil, used occasionally, good dehydrating agent.

Cedar wood oil, one of the best, penetrating well, not making tissues brittle as clove oil does.

Sectioning.—Paraffin preparations are cut dry, no alcohol or other fluid being used on the knife, and the blade is usually at right angles (to the long axis of a sliding microtome); if of the right consistence the sections are even and uniform and do not roll; for further handling they may be fastened to a slide or a cover-glass by either of these two methods :

Float the sections on water at 45° C. in a rather large and shallow vessel; they smooth themselves out and may be picked up by sliding a perfectly clean glass slip under them, tilting to let the water flow away, or lightly touching with bibulous paper or pressing with the finger tip, then laid in the thermostat at 37° C. for 2 to 3 hours; or more rapidly, dried on the slide by holding it over a flame till the paraffin *begins* to look transparent. Or

Egg albumin is whipped and filtered, equal quantities of glycerin added, a slide very thinly coated and then heated to

about 70° C.; cool, float a film of distilled water on the slide, lay the section on this, warm slightly if wrinkled, dry off water by filter paper, lay in thermostat 3 to 4 hours.

Before staining the section the paraffin may be removed by 5 to 10 minutes treatment with chloroform, xylol or turpentine oil, then in absolute alcohol 10 minutes; any desired method of staining may then be employed. Often the staining is quite as effective if the paraffin be not removed. Extra thin sections may be cut if a very little thin celloidin be brushed over the face of the block before each section is cut, but great care is needed not to use too much or to put it on the vertical side of the block; each section as cut is laid on a slide with albumin fixative, celloidin surface down; meanwhile the coating on the next is hardening.

Serial Sections.—With a square set knife and a paraffin at about 45° C. melting-point, in a room temperature about 17° C., the edges of the block being pared away as much as possible and the front and back edges straight and parallel, with a very rapid stroke a series of sections may be cut, each of which clings lightly to the one just before and the one just after it, so that a ribbon is formed; large divisions of this, containing many sections, may be picked up and handled at once, stained and mounted, making it possible to study the entire thickness of the tissue as section after section is passed in review. It is well to receive the ribbon as it is cut upon pieces of toilet paper, and if perfect they may be mounted at once. If they show wrinkles or tend to roll they must be expanded, as also when the section is smaller than the cut surface of the block. For this purpose they are floated in groups on the surface of warm water or alcohol, or a number of them placed on a water film on a slide and heated, the water absorbed by blotting paper and the sections fixed in the thermostat or over a flame.

When fixed on the slide the paraffin may be removed by either benzol, chloroform, toluol or xylol; various mixtures of these may be used, as also hot alcohol, creosote, turpentine and clove

oil. The slide may be warmed till the paraffin begins to melt and at once plunged into a tube of xylol and mounted from it, or the xylol may be removed by alcohol and the sections stained.

Recapitulation of paraffin for small objects :

1. Enough cedar oil in a test-tube to cover the tissue.
2. Pour on the same amount of absolute alcohol.
3. Put the dehydrated tissue into the alcohol and wait till it sinks to the bottom of the oil ; when the wavy lines at the junction of the two fluids have vanished, put the tissue into
4. Low melting-point paraffin ; change once or twice.
5. Float the vessel on cold water when the tissue is filled with paraffin, when hard, cut a block containing the tissue and
6. Mount on a cone of harder paraffin already on the object-carrier of the microtome.
7. Cut serial sections, if desired, with thin collodion if necessary.
8. Flatten the sections on warm water.
9. Float them on a slide.
10. Remove paraffin, stain, mount.

Celloidin Method.—Two grades of celloidin solution in equal parts of ether and alcohol are used, one of about the consistency of ordinary mucilage and the other as thick as molasses. The tissue is well dehydrated in absolute alcohol, laid in equal parts ether and alcohol till quite saturated (1 to 3 days), then put in the thin solution for 24 hours, and an equal time in the thick, but if there is no haste a longer time in each celloidin will be advantageous. For sectioning, the well impregnated tissue is mounted on blocks of glass or wood (cork is too yielding), and for wood the plugs used by shipbuilders to conceal the nails in decks, hence called "deck plugs," will be found useful. A film of celloidin is placed on the plug ; before it is quite dry the tissue is placed upon it and allowed to become firm, which takes but a few minutes, a little more celloidin is poured on and about the

tissue, building it up, and when the surface is fairly hard the whole is laid in chloroform or 80 per cent. alcohol till hard enough to cut ; if the hardening on the plug is conducted slowly under a belljar to prevent too rapid evaporation of the ether, the result is better. Or a number of bits of tissue may be laid on the bottom of a shallow glass vessel, celloidin poured over them, the vessel covered loosely, and the cake formed in 12 to 24 hours cut and mounted as desired.

In cutting, the block of wood and tissue is clamped in the object holder of the microtome and the blade is set as slanting as possible consistent with sweeping the entire surface of the object ; 80 to 90 per cent. alcohol is used to keep the blade as wet as possible, a thick camel's hair brush being convenient for the purpose and also to lift the sections as they are cut into a vessel of water, where they flatten out, or into alcohol. After staining the section, if clove oil is used to clear, it dissolves the celloidin, which allows delicate tissues and thin sections to fall apart ; oil of origanum (*cretan*, *not gallic*), oil of bergamot, oil of cedar, or xylol with carbolic acid do not dissolve the celloidin. The latter is made thus :

Xylol,	3.0
Ac. carbolic cryst.,	1.0

For dehydration of sections a mixture as follows may be used :

Chloroform,	1 part.
Absolute alcohol,	2 parts.

If necessary to remove the celloidin, as often after the use of anilin stains which stain also the celloidin, put a few drops of clove oil on the section on a slide, after five to ten minutes remove the oil with a pad of bibulous paper and pour a few drops of xylol on the section : balsam, cover-glass.

Recapitulation of celloidin method :

1. Dehydrate with absolute alcohol.
2. Ether and alcohol, equal parts, 1 to 3 days.
3. Thin celloidin 1 to 5 days.

4. Thick celloidin 1 to 5 days.
5. Fasten on wooden plugs and dry 15-20 min.
6. Chloroform 2 to 5 hours ; vapor of chloroform 12 hours or 80 per cent. alcohol 12 hours.
7. Cut wet with slanted knife.
8. Stain, clear with oil of origanum, etc.
9. Mount in balsam.

Keep the balance of the tissue on the plug in 80 per cent. alcohol, or pry the imbedded mass off the block and keep that in alcohol, labelled properly.

Combinations of paraffin and celloidin have been recommended but either method alone is satisfactory as soon as the details are familiar, if a little care is used ; for pathological purposes the combined method is hardly necessary. It is as follows :

Imbed in celloidin.

Soak the imbedded material in oil of origanum (cretan)
12 hours or more till quite transparent.

Concentrated solution of paraffin in origanum oil 12
hours, heating to 40° C.

Melted paraffin at 50 to 52° C., 12 to 24 hours.

Harden, pare and mount on firmer paraffin, cut, etc.

Glycerin-jelly Method.—This method is rapid but does not permit very thin sections. The hardened tissue is left 24 hours in thin mucilage (made with gum arabic) and glycerin, equal parts ; then laid on a block, put in alcohol when firm, cut and stained ; water, especially if slightly warmed, removes the imbedding mass.

D. Staining Methods.—The principle upon which the technique of staining depends is that certain cells and parts of cells display a special affinity for certain dyes, thus becoming prominent in the section and permitting closer study ; but it must never be forgotten that a stained tissue is not strictly a normal picture, and hence it is well as a matter of routine to examine unstained preparations both before and after other similar sections are stained, in order to correct and supplement the details brought

out by the dyes. Certain anilin and other colors stain nuclei especially well, others color the cell body or the interstitial substance; by combining two or more we obtain polychromatic pictures of the greatest value; if a single stain colors different tissue elements different colors in one staining it is called metachromatic, as gentian violet and methyl violet, which stain amyloid material red and the rest of the tissue blue-violet. From a chemical standpoint the stains are divided into basic, neutral and acid; in the first the staining element acts as a base, combining with acid cell constituents (nucleo-phosphoric acid?) like fuchsin and magenta; the acid stain is one where the coloring agent acts as an acid, like acid fuchsin; neutral stains are usually made by artificial combinations of acid and basic stains. In a general way the basic stains are nuclear or chromatin stains, and the acid are cell or plasma stains; both usually require differentiation after their use, that is, if a nuclear stain has been employed the cell body is lightly and diffusely colored while the nucleus is deeply stained and the color must be removed from the plasma in order to make the nuclei clearer. (See Pt. II., Chap. I., appendix.) As decolorizers we may use distilled water, alcohol, anilin oil, weak acid in water or alcohol, and weak alkaline solutions.

General rules:

1. Good staining requires the tissue to be properly fixed and hardened; fresh material and tissue left too long in alcohol or chromic acid and its mixtures may not stain at all.
2. Staining materials must be of the best, obtained from some reliable firm, carefully prepared, and always filtered before use to avoid precipitates in the tissue.
3. Sections should be properly spread out in relatively large quantities of the stain and should not lie upon each other, so that the fluid reaches their surfaces unequally.

4. As to the rapidity of staining solutions and combinations, only the indefinite statement may be made that old and ripened stains usually are quicker than those freshly made ; but the previous treatment of the tissue is also of importance.
5. The staining power may be increased by
 - (a) Strengthening the concentration of the dye.
 - (b) Heating to 30 to 40° C.
 - (c) Adding mordants, like acids and alkalis, alum, anilin oil, etc.
6. Decolorizing agents must be entirely washed out after use or the stain rapidly bleaches in the mounted preparation.

Nuclear Stains.

Carmin.—This gives good and lasting stains but the solutions are liable to spoil after keeping a short time.

1. *Alum Carmin :*

Carmin,	1 gm.
5 per cent. alum solution,	100 gm.

Boil 20 minutes, cool, filter ; good for tissue hardened in alcohol, sublimate, Müller's fluid, and formalin.

Sections from distilled water :

- (a) In the stain 10 min. to several hours ; overstaining does not occur ;
- (b) Washed several times in distilled water ;
- (c) Mounted in glycerin or carried through alcohol, oil and balsam.

Nuclei are red with a bluish tinge, cell body pale.

2. *Lithium Carmin :*

Carmin,	2.5 gm.
Sat. sol. lithium carbonate,	100 gm.

Combine, with a mild degree of heat if necessary, cool, filter; good for tissue hardened as above.

Sections from distilled water:

(a) In the stain 5-10 min.; paraffin sections a little longer.

(b) Well washed.

(c) Differentiated in alcohol (70 per cent.) 100 parts, hydrochloric acid 1 part, 5-10 min.

(d) Wash thoroughly.

(e) Mount in glycerin or alcohol, oil, balsam.

Nuclei deep red, the other tissue elements pink or colorless according to the differentiation. This stain may cause the tissue to swell badly because of the large per cent. of alkali; paraffin sections should be fastened to the slide first.

3. *Borax Carmin*:

Carmin,	0.5
Borax,	2.0
Distilled water,	100.0

Mix, boil, stir constantly with a glass rod and add drops of 0.5 per cent. acetic acid till deep red color is obtained; let stand 24 hours, filter.

Tissue hardened as above.

Sections from distilled water:

(a) In stains 5 to 20 minutes.

(b) Washed.

(c) Differentiated in hydrochloric acid and alcohol as above.

(d) Thorough washing.

(e) Alcohol, oil, balsam.

Nuclei are red.

Hematoxylin.—This is one of the best and most generally used of the non-anilin stains; good for usual hardenings, except after chromic and osmic acids and mixtures, but Delafield's

hematoxylin gives good results with long staining. None of the hematoxylin mixtures are active when first made, having to go through a ripening process of several days to weeks; as this is essentially an oxidation by which hematein is formed, the addition of hydrogen peroxide to the fresh stain accomplishes the same result without loss of time. The strength, that is, staining power, increases with age, hence a moment or two will be long enough with an old solution and 15 to 20 minutes may be needed for a recent one. Filter the stain each time before use; afterward return it to the bottle through a filter, as it may be used again indefinitely. Sections when once stained may be washed in water from 30 minutes to several hours, and if there is a little alkali present (less than 0.5 per cent.) the differentiation is more complete. Nuclei are deep blue, plasma bluish, according to the differentiation; mucus, lime salts and cartilage are also stained. Excess stain may be removed by the following, and sometimes it is well to overstain on purpose and control the decolorization till the desired color is reached:

Hydrochloric acid alcohol as given above, well washed out with ordinary water; usually 30 seconds to 3 minutes is long enough to clear up any but the deepest overstaining. The color turns reddish brown in the acid, becomes blue again in water. A few drops of saturated lithium carbonate solution hasten the removal of the acid.

Alum in 0.5 per cent. solution is slower than the acid alcohol, but for that reason it is easier to obtain any desired depth of stain.

The following are the commoner hematoxylin solutions used in pathology:

1. *Böhmer's*:

- | | | |
|----|-------------------------|---------|
| A. | { Hematoxylin (cryst.), | 1 gm. |
| | { Absolute alcohol, | 10 cc. |
| B. | { Alum, | 20 gm. |
| | { Hot distilled water, | 100 cc. |

Filter while hot.

After standing 24 hours the two solutions are mixed and ripened for a week in open wide-mouthed bottles.

2. *Delafield's* :

Hematoxylin (cryst.), 4 gm.

Absolute alcohol, 25 cc.

Dissolve and add to

Saturated ammonium alum, 400 cc.

Ripen 5 to 7 days in unclosed bottle, frequently stirring with glass rod, then add

Methyl alcohol, 100 cc.

and preserve in well-stoppered bottles. For use, take equal parts of stain and distilled water.

3. *Friedländer's* :

Hematoxylin (cryst.), 2.0

Absolute alcohol, 100.0

Distilled water, 100.0

Alum, 2.0

Glycerin, 100.0

4. *Ehrlich's acid hematoxylin* :

A. { Hematoxylin, 2.0
Absolute alcohol, 60.0

{ Glycerin, 60.0
Water, 60.0

B. { Alum to saturation,
Glacial acetic acid, 3.0

Mix, ripen in open vessel a week, keep in well-stoppered bottles and precipitates seldom form, overstaining even with old solution not common.

Sections from distilled water :

(a) In stain 3 to 10 minutes, less with old stain.

(b) Washed 30 minutes to several hours.

(c) If overstained, use acid alcohol or alum solution.

(d) Wash out well.

(e) Mount as desired.

5. *Mayer's hematein* :

A. {	Hematein,	1.0
	Alcohol, 90 per cent.,	50.0

Dissolve with heat.

B. {	Alum,	50.0
	Distilled water,	100.0

Mix A and B, cool, filter. Gives very deep stain at once, does not require ripening; with the addition of glacial acetic acid (2 per cent. of the entire mixture), very satisfactory results are obtained.

Anilin Stains.

Tissues which have been hardened in chromic acid or its salts may not take the stain, otherwise the action is quick and simple; many of these do not last very long, the tissue bleaching out even when kept in the dark, and glycerin mounts are the least durable. Solutions seldom remain active for longer than a few weeks and should be filtered before use; bacteria grow freely in some solutions and should be controlled by the addition of a few drops of carbolic acid.

1. Bismarck brown or Vesuvin :

Vesuvin,	2.0
Alcohol (90 per cent.),	60.0
Distilled water,	40.0

Heat to boiling, cool, filter, add 5 per cent. carbolic acid solution, 10 drops.

Sections from alcohol :

(a) In stain 5-10 min.

(b) Washed in alcohol.

(c) Mount in balsam after clearing: or in glycerin, which does not destroy this stain.

Nuclei brown, plasma lighter, mucus and bacteria stain also.

2. Gentian violet :

Gentian violet,	2.0
Distilled water,	100.0

Heat, cool, filter. Methyl blue is prepared in the same way. For other combinations see pp. 302-3.

Overstaining, especially with gentian violet, very apt to happen but may be corrected with plain or acid alcohol. Mount in balsam.

3. *Fuchsin* :

Fuchsin,	1.0
Alcohol (40 per cent.),	100.0

Heat, cool, filter. Use as for vesuvin. The addition of 2 per cent. acetic acid gives a good stain for fresh material, not hardened, and may be carried under the cover-glass by blotting paper.

4. *Safranin* :

Safranin,	1.0
Alcohol (30 per cent.),	100.0
Distilled water,	200.0

Heat, cool, filter ; dilute one half for use.

Sections from alcohol.

(a) In stain up to 24 hours.

(b) Washed in water.

(c) Washed in acid alcohol—HCl 6-8 drops, or saturated picric acid in water, 10 drops ; alcohol, 100 cc.

(d) Washed in absolute alcohol till no more clouds of stain are withdrawn.

(e) Cleared in oil or xylol, mounted in balsam.

Resting nuclei are pink, mitotic figures deep red, mucus yellowish-red, fibrin (after Flemming's hardening fluid) deep red.

For more rapid results :

Safranin in excess,	
Distilled water,	100.0
Anilin oil,	2.0

Heat to 70° C., filter through wet paper. The stain is almost instantaneous, used as above.

Diffuse and Double Staining.

Diffuse staining occurs in pathological technique as contrast stain for all tissue elements except nuclei, the latter being of a deep and different color and hence more prominent on the diffuse background; thus blue and violet nuclear stains are used with a reddish plasma stain, red nuclei are displayed on a yellow background; the nuclei are usually stained first in stronger fluid and then the weaker contrast is used.

1. *Ammonia Carmin* :

Carmin finely powdered,	1 part.
Aq. ammon. fort.,	1 "
Distilled water,	75 parts.

Mix, allow the ammonia to evaporate, filter, ripen several weeks before use. Keep tightly corked as the solution becomes rapidly moldy. This stain may be prepared by rubbing the carmin and ammonia together in a large glass mortar, spreading the thick mass over the whole inner side to dry, then repulverized, allowed to stand 24 hours in an open vessel, and dissolved for use in cold distilled water: this is ready immediately, requiring no ripening. Staining power increases with age.

To use, add the stock solution by drops to distilled water till pale red; in this put sections from distilled water for 12-24 hours; wash, dehydrate, clear and mount. Stronger solutions are quick but indistinct in results. Sections are best stained if laid flat on bibulous paper, not allowed to cover one another. Heating to 40-50° C. is necessary for tissues hardened chromically.

Nuclei, plasma, fibrous tissue, muscle fibers of both kinds, decalcified bone, neuroglia, axis cylinders and hyaline material will be stained; elastic tissue, basement substance of hyaline cartilage, nerve sheaths, mucus, fat, and corneous epithelia are unstained. Hematoxylin stain first is to be recommended.

Picric Acid.—A few drops of saturated alcoholic or aqueous solution added to distilled water, sections treated for a short time (up to 5 min.), washed in water or alcohol, if too much stained decolorized in 1 part saturated solution lithium carbonate to 10 distilled water. Plasma, red cells, muscle cells, fibrous tissue, fibrin, hyalin, corneous epithelia are stained yellow.

Picric acid is seldom used alone. With hematoxylin and safranin it partly removes the first stain, hence overstain before putting sections into the picric acid. Among the combinations of this kind micro-lithium carmin is one of the best:

Lithium carmin solution, 1 to 1½ parts.

Picric acid, watery solution, 2 “

Or Friedländer's mixture may be used:

Carmin, 1 part.

Liq. ammon. fort., 1 “

Distilled water, 50 parts.

Stir and add, a drop at a time, saturated watery picric acid solution, 1-4 parts according to the percentage of ammonia present: filter and add 10 drops carbolic acid. Stain 5-10 min., wash, decolorize with acid alcohol 2-5 min., wash in distilled water 10 min., alcohol, oil, balsam.

Eosin.—This is the commonest contrast stain after hematoxylin, used in 0.1 to 1.0 per cent. in alcohol, acts very quickly but the excess easily comes out in alcohol. Tissue fixed in formalin or sublimate, stained in hematoxylin, decolorized in acid alcohol, washed in several waters, stained in 1 per cent. eosin in alcohol, again washed in water and allowed to lie in water till no more red is apparent to the naked eye, dehydrated

and mounted in balsam ; the erythrocytes are brilliant red and the tissue resembles a fine injection as the vessels are everywhere prominent, eosinophile cells are easily found. The eosin can be put in the clove or origanum oil used for clearing, but better results are obtained as above.

Biondi-Heidenhain method :

Methyl green, saturated aqueous solution,	50.5
Orange, saturated aqueous solution,	100.0
Acid fuchsin, saturated aqueous solution,	20.0

The separate solutions stand for a few days with excess of dye before mixing ; for use one part is diluted with 100 parts distilled water. A drop of this on a filter paper makes a spot which is bluish-green in the middle, orange on the circumference, if there is a zone of red external to this too much fuchsin is present. Harden in sublimate, imbed in paraffin ; if the tissue has lain long in alcohol, wash it in 0.1 per cent. of acetic acid 1 to 2 hours, then in water.

Sections from distilled water in stain 24 hours, 90 per cent. alcohol 1 to 2 minutes, dehydrate rapidly in absolute alcohol, xylol, balsam.

Resting nuclei are bluish-green, dividing nuclei and fragmented leucocytes are deeper blue-green, plasma and fibrous tissue are red, erythrocytes are orange-red, fibrin red, mucus green. Method unreliable, and color soon lost from nuclei.

Van Gieson's method.

Tissue hardened in alcohol, formalin, sublimate, Müller's fluid ; cut, overstained in Delafield's hematoxylin, well washed ; then 3 to 5 minutes in :

Saturated aqueous picric acid,	150 cc.
Acid fuchsin solution,	3 cc.

Wash in water half a minute, dehydrate, oil, balsam. Nuclei deep brownish-red, fibrous tissue and hyaline (of epithelial origin) red, muscle cells red, remaining tissue yellow.

E. Bacteriological Methods.

Sterilization.—Every utensil, test-tube, knife and culture-vessel must be free of bacteria, or the results obtained cannot be trusted. To obtain this required cleanliness two methods of sterilization are employed: by heat and by chemical solutions. Heat is applied as dry or as moist heat. The former requires that objects to be sterilized be kept at a temperature above 100° C. for a relatively long time, and as the power of penetration of dry heat is limited, the method is reserved for glass plates, knives, small dishes and other utensils which are not injured by the high temperature. The articles to be sterilized are placed in a hot-air oven of Swedish iron, double-walled, with a double door and a bottom of heavy copper, and kept for at least an hour at 100° to 150° C., or even 180° C., and under this heat, supplied by Bunsen burners, the copper plates which form the bottom are apt to be burnt out in time; the oven should be well jacketed with thick asbestos to lessen the radiation.

Moist heat is more commonly used for sterilization, usually as flowing steam; its power of penetration is greater, and it may be used at a lower temperature than dry heat with less damage to the articles in the oven; by an arrangement which supplies the steam under extra pressure, the penetration and degree of heat increase with good results where clothes and other fabrics require to be treated. In the laboratory the various fluids and solids used as culture media would be ruined if sterilized at the high temperature of the dry method, and many spores resist the dry, while they succumb readily to the moist heat.

The application of the heat varies with the method. Dry heat is always continuously applied till the objects are sterilized. With steam the fractional method is more often used. The principle is that a short exposure of a culture medium to flow-

ing steam will destroy all the mature bacteria which may be present, but perhaps not the spores; the latter are given time to develop at ordinary room temperature, and the medium is for the second time exposed to steam and any bacteria which may have developed in the interim are destroyed; a second repetition is usually required, and in some cases even more. The media would be rendered sterile if exposed for hours at the same temperature, and the spores either would not develop or die in the process, but the medium, being composed of organic materials, such as gelatin, milk, broth, etc., would be rendered unfit for the future growth of bacteria in them, hence the value of the fractional method. The custom is therefore to expose the media to steam, in test-tubes and other containers, for fifteen to twenty minutes, on three succeeding days, at about the same hour.

Fractional sterilization at a low temperature is carried out in the same way, but the temperature is regulated at about $65-70^{\circ}$ C., and this method is used where the substance to be treated will not endure a high degree of heat, as in the case of blood serum; an hour's exposure being given for three days and the material kept at about 30° C. between times.

A third way of using steam, under pressure of at least one additional atmosphere, which is equivalent to raising the temperature to 122° C., and which will usually destroy all bacteria and their spores in less than half an hour, is sometimes employed in the laboratory, more often in disinfection for hygienic purposes. It is difficult to control the time of the exposure by this method, for when the required degree has been reached it will not do to open the autoclave, since the sudden relief of pressure causes the fluids to escape from their containers; articles must thus be exposed while the temperature is rising, for the required time at the proper degree, and also while the oven cools enough to permit opening it.

As used in the laboratory the forms of steam sterilizer resemble the original oven designed by Koch, and consist of a metal cylinder, the lower part containing a reservoir for water and a

protected space for the application of heat, the upper and larger portion being double-walled or jacketed with felt for the prevention of radiation, and communicating freely with the water chamber for the reception of the steam. Objects are placed in the upper part, tightly covered, heat applied below, and steam allowed to flow through the apparatus for the desired time; the water chamber has a gauge to show the amount of water present, and unless the supply is copious the bottom may burn out. An Arnold steam sterilizer may also be employed for ordinary work.

When the sterilizer has a tight-fitting cover, which may be screwed down so that no steam can escape, and a safety valve on top for control, it is called an autoclave, and works on the principle of steam under pressure, as above.

Knives, forceps, slides and platinum loops may be sterilized by holding them for a short time in the flame of a Bunsen burner.

Chemical sterilization is seldom used except for utensils, as the chemicals would injure media and prevent the growth of bacteria. The commonest solutions used for chemical sterilization, with their strengths, may be seen by referring to Table of Antiseptic Solutions, p. 314.

These fluids act by forming chemical combinations of unknown constitution with the substance of the bacteria, but even corrosive sublimate, one of the strongest, may not kill the bacteria, for if the mercury salt is removed within a short time the germs may be able to go on living.

Culture Media.—These may be either natural or artificial, fluid or solid:

	<i>Natural Media.</i>	<i>Artificial Media.</i> *
Fluid	Blood serum,	Mixed chemical solutions,
	Hydrocele and ascitic fluid,	Beef and other broths,
	Urine,	Vegetable infusions.
	Eggs, uncooked,	
	Milk.	

	<i>Natural Media.</i>	<i>Artificial Media.</i>
Solid	Blood serum, coagulated,	Broth or
	Potatoes,	Milk with a solidifying
	Eggs, cooked,	substance added, as
	Sterilized organs.	Gelatin or agar.

1. **Natural Media.** *Blood Serum, Fluid.*—Blood is drawn from a healthy animal at the time of slaughtering by incising a vessel and allowing the blood to pass into a sterile jar ; the latter is covered and put in a cool place and the clot allowed to form, a sterile glass rod gently detaching it from the side if necessary ; when coagulation is complete the clear serum may be siphoned off into sterile test-tubes or other containers. If everything has been sterile the serum is safe to use, either fluid or solid, without sterilization.

2. *Blood Serum, Solid.*—Siphon off the serum into sterile test-tubes, a few cc. in each, lay these in a hot-air sterilizer, slanted, and raise the temperature to 80° C., not higher ; the serum sets and is clear straw color, opalescent ; the tubes are then sterilized at 100° C. in steam thirty minutes a day, three days.

Löffler's serum mixture :

Broth with 1 per cent. glucose,	1 part.
Serum,	3 parts.

Mix, fill tubes, raise to 65° C. an hour a day for three days, or sterilize as above ; good for many kinds of bacteria, especially diphtheria.

3. *Eggs* may be sterilized by the low temperature method and a small hole made in one end by a sterile instrument, inoculated through the opening and closed with wax or paraffin ; if dipped in paraffin there is less evaporation of contents.

4. *Milk*, deprived of its cream by standing in a cylindrical vessel and then drawn off by a stopcock at the bottom, or "separator" milk from butter factories, sometimes is useful, as certain bacteria coagulate it or peptonize it ; with a little litmus added the reaction of the growing bacteria is apparent. Test-

tubes are charged with it and sterilized in steam three days ; care and thoroughness especially necessary as milk when delivered is usually full of bacteria and their growth is rapid.

5. *Urine* may be occasionally used, as also hydrocele and pleuritic or ascitic fluid, but generally the ordinary media are quite sufficient.

6. *Potatoes* are of great value in routine laboratory work. They should be of medium size, free from bruises and spots ; scrub them well with a brush and ordinary water, then with 1 to 1,000 bichloride solution, rinse in sterile water and sterilize in steam for an hour for three days or in the autoclave half an hour. Cut across with a sterilized knife they may be inoculated on the smooth surface and the bacteria developed in the thermostat, the potato lying in a sterile dish with a cover ; or before sterilizing a series of semicylindrical pieces with one slanting side may be cut, these slipped into test-tubes with a few drops of water and sterilized in steam by either method. Other vegetables may be used, as carrots, but the potato is sufficient.

7. *Various organs* of lower animals may be sterilized and used for streak cultures, and human skin, freshly obtained after death and treated with digestives (pepsin, pancreatin), is at times useful. Cat kidneys halved and sterilized will serve for some difficult bacteria (streptothrix).

Artificial Media.—A good example of a complex chemical substitute for albuminous fluids is

1. *Uschinsky's medium* :

Ammonium lactate,	6 to 7 gm.
Calcium chloride,	5 to 7
“ phosphate,	2.5 to 3
Magnesium sulphate,	0.2 to 0.4
Sodium chloride,	5 to 7
“ asparaginate,	3 to 4
Glycerin,	30 to 40
Distilled water,	1,000 cc.

Mix, put in tubes, sufficient in each, sterilize in steam.

2. *Dunham's peptone solution :*

Pure peptone,	10 gm.
Sodium chloride,	5 "
Distilled water, to make a paste.	

Rub well in a mortar and afterward dilute to 1,000 cc., boil and filter, sterilize ; it is ready for use and is employed to test for indol in growing cultures.

3. *Potato Extract*.—Rub 500 gm. potato with 500 cc. distilled water, decant, dilute to 1,000 cc., add 40 gm. glycerin ; good for tubercle bacilli.

4. *Hay, malt and other vegetable infusions* have been used for particular purposes but find little application in ordinary bacteriological work.

5. *Beef Broth ; Bouillon*.—Of all fluid media this is the commonest and most useful. It is made by soaking lean beef, free from gristle or fat and chopped fine in a mincing machine, half a kilo (about one pound) in 1,000 cc. water 12 hours ; squeeze the meat in a coarse towel and filter the total liquid obtained. Add sodium chloride 10 gm. and peptone 5 gm. Test for reaction and slightly alkalize by sodium hydrate solution, 10 per cent., added in drops ; litmus will do for the test but phenolphthalein is better, 1 gm. dissolved in 1,000 cc. 50 per cent. alcohol. To use, several watch glasses are arranged in series with 1 cc. of the solution in each ; a drop of the broth is added to the first, more sodium solution is added to the broth and another drop tested ; when alkaline the test solution turns rosy red. At this point salts and proteids insoluble in alkaline media precipitate and broth becomes cloudy ; it may be necessary to boil and filter and alkalize again. For tubercle bacilli 6 per cent. glycerin may be added to this alkaline bouillon. Various bacteria cloud this medium or form a film on the surface or change the reaction or fall as a light cloud to the bottom. To use in a solid form, glycerin and agar are added to the broth.

6. *Beef Peptone Gelatin*.—To 1,000 cc. cool broth add in small pieces 100 gm. "gold leaf" gelatin, soak twenty minutes or till well swollen, dissolve by gentle heat on a water-bath, remove and cool to 50° C., alkalize with great care; if too alkaline it will not set, correct by a few drops of 5 per cent. acetic acid, the reaction must be faintly alkaline. Now mix a broken egg, shell and all, into the medium and boil half an hour over a flame covered with wire gauze, adding water as it evaporates. Try it by putting a little in a test-tube and repeatedly boiling, if still clear and right in reaction, filter the rest into test-tubes, sterilize, and properly cork with cotton. It is perfectly clear when well made and solid below 22° C. Certain bacteria produce a proteolytic ferment which liquefies this medium.

7. *Beef Peptone Agar*.—Small pieces of agar, 10 gm. in all are added to 1,000 cc. cold bouillon, boiled an hour with frequent stirring, water added as required and the whole filtered. In filtering both gelatin and agar a jacketed filter is sometimes used, kept hot by a Bunsen burner, but this entails evaporation and thickening of the medium and is not necessary if the solution is perfect and if a little is added at a time to the filter, the rest being kept hot on a water-bath. The fluid should be poured carefully along a glass rod onto the side of a carefully folded filter paper. Gelatin must not be boiled too long or it will not set; agar may be boiled indefinitely but may stick to the vessel. Agar is not so clear as gelatin but it is solid below 42° C. and hence may be put in the thermostat at body temperature, which is optimum for many bacteria. Various mixtures may be employed, glycerin, neutralized urine, glucose, lactose, etc., for special purposes.

Instead of beef or veal for these media, Liebig's or Armour's extract of beef may be used.

To Clean and Fill Test-tubes.—Fasten a wad of cotton on the end of a strong glass rod, dip in nitric acid and swab the inside of the tube, rinse four times in water, drain, and, when nearly dry, rinse with 95 per cent. alcohol, dry, sterilize. Plug the

tubes with cotton and sterilize in hot air at 150° C. till the cotton turns brownish. By a short rubber tube connect a filter and a short glass tube, a pinch-cock on the rubber part ; insert the end of the glass tube part way down a test-tube and release the pinch-cock till 5-8 cc. broth or other medium are in the tube, shut off, re-apply the cotton plug, sterilize three times in half an hour in steam. The fluid must not touch the rim of the test-tube or the cork will stick. Other vessels, Erlenmeyer flasks, etc., may be treated in the same way. If the cotton plugs are covered with tin foil while in the sterilizer the steam does not condense upon them ; covered with rubber caps they do not dry out on long keeping. Having prepared tubes with gelatin, agar and serum allow some of them to lie at a slant so that when set they will present a broad surface for inoculation ; others are kept upright for stab cultures. If laid for 24 hours nearly horizontal at room temperature the gelatin and agar slants will not slide down in the tubes. If the tubes are wanted for anaërobic cultures they must be half filled with the medium that the bacteria may develop in the depth away from the air.

Kinds of Cultures.—The usual forms of cultures are :

1. Stab.
2. Slant.
3. Plate.
4. Petri dish.
5. Esmarch roll.
6. Hanging drop.
7. Anaërobic.

The first is made by holding a platinum wire, fused to one end of a glass rod, in the flame till it glows ; with this sterile wire, which may be straight and slightly flattened or looped at the end, some of the material to be studied is picked up, the cotton plug of a sterile and charged tube is held between the fingers of the left hand while the tube itself is held by thumb and first finger, the loaded needle is sunk straight to the bottom of the solid gelatin or agar or stirred about in fluid media ; the

stab must be straight and in the mid axis of the tube and the needle should not be allowed to touch the side; the cork is replaced, the platinum wire is again heated in the flame; before and after charging a tube thus the cotton plug is set on fire for a moment and the opening of the tube passed through the flame, to destroy chance germs. Such a tube is then incubated at room temperature if containing gelatin or in the thermostat at constant temperature if agar or serum or broth; when it contains but one kind of microorganism and its brood it is called a pure culture, otherwise it is a mixed or contaminated culture. Slant surfaces of solid media, agar, serum, potatoes, etc., are inoculated in a similar way by drawing the charged loop over them.

For plate cultures small squares or oblongs of glass are sterilized in hot air; three tubes of gelatin or agar are melted and kept in a water-bath; matter to be studied is introduced into one, a platinum loop or two of this fluid medium with bacteria, is used to make a dilution in the second tube, a loop or two from the second inoculates the third; the needle flamed between each two; the tubes are marked in chalk or by labels with the date, kind of material, and the number of each; a sterile plate is laid on a larger piece of glass which in turn rests on the surface of cold water in a container, the melted inoculated medium of tube No. 1 is poured carefully on it and guided with a glass rod so that it sets with a margin of clear glass all about it—this film when solid again presumably contains many and probably different bacteria scattered singly over the plate and where they are lodged each will develop into a colony. But as the first plate usually contains altogether too many colonies, dilution No. 2 makes plate No. 2 and dilution No. 3 makes plate No. 3, and one of these latter will contain so few colonies, when incubated, that different kinds may be recognized, lifted out bodily with the broad ended platinum wire, and used to make a pure culture in a new tube. When the three plates are poured and set they are piled one on the other, No. 1 lowest, each separated from the others by little glass bridges, and the whole in a sterile dish with

a cover, and at the end of 12-24 hours in the proper temperature they are ready for examination.

Such plates have been nearly given up in favor of similar cultures in the Petri dish, a shallow glass dish with a cover, which may be set on the stage of a microscope and examined without removing the cover and risking contamination by matter floating in the air.

Another device is the rolled culture or Esmarch tube. A test-tube of melted medium is inoculated, laid on a block of ice with the stopped end but little higher than the other, and rotated, slowly at first then rapidly; the film sets all round the inside and bacteria develop where caught and the unopened tube may be examined by a magnifying glass or the low powers of the microscope.

The hanging drop culture is made by using perfectly clean hollow ground slides; a ring is made with vaselin round the depression in the slide; a cover-glass is sterilized and laid on a wire gauze under a belljar; in the middle of the cover-glass a drop of beef broth is placed, this is inoculated with any desired pure culture, the platinum needle being flamed and allowed to cool between placing the drop and inoculating it; and afterward the cover-glass is then carefully reversed over the ring of vaselin, slightly pressed to shut out the air, and the preparation set away in a moist chamber at 37° C. to incubate; in 12-24 hours it may be studied with the higher powers.

An anaërobic culture may be made by deeply inoculating a tube more than half full of solid medium, the germs developing in the deeper portion away from the air; or melted paraffin may be poured on the top of the medium, or oil, to shut out oxygen; or a stream of hydrogen may be passed into the tube and the glass tube by which it enters closed by a flame.

Inoculation of Animals.—Mice may be inoculated with any pure culture or suspected material by cutting a small pocket in the skin just over the root of the tail, after clipping the hair close, and depositing it within the pocket or farther from the

wound along the back ; special mouse holders are sold for the purpose. Or a hypodermic syringe carries the inoculated broth culture into the peritoneal cavity, after clipping and disinfecting the skin and sterilizing the needle. Rabbits, guinea-pigs, pigeons and other small animals may be used similarly, an assistant holding them quiet while a surface of skin is cleaned and the inoculation practiced. The rabbit is often inoculated through the anterior branch of the large vein of the ear, directly into the circulation. When solid pieces of tissue are introduced into the serous cavities of animals a careful surgical operation must be done, with complete asepsis, and the wound carefully closed and dressed. After inoculating an animal note and record at regular periods its temperature, loss of weight, position in the cage, appetite, diarrhea, reaction at the site of inoculation, etc. After the death of the animal make the post-mortem immediately and if delay is unavoidable always note in the record the exact amount of time elapsed. Make the external inspection, weigh, fasten on a sterile board with tacks or small nails, wash the whole body with 1-1,000 bichloride and rinse this off with sterile water. Apply (while still hot) a broad bladed knife which has been heated red to the linea alba and transversely across it, open through the charred lines, the skin only, and reflect and tack it to the board. The track of all incisions must be charred superficially in this way before opening ; in making cultures from an organ a scalpel is reddened in the flame, laid on the organ, again heated and used to cut through the char, a platinum loop passed deep into the organ through the cut and twisted to gather some of the uncontaminated cells and fluids, and this is inoculated into any desired medium ; instead of the loop the spade end may be used. Cover-glass preparations should be made at the same time from blood and exudates. For further study the organs may be cut out with sterile scissors and dropped into 95 per cent. alcohol or 3-5 per cent. formalin, imbedded, cut and stained. A careful record of the autopsy as a whole and of the organs from which smears and cultures are made must be kept.

Staining Bacteria.

A few of the basic anilin colors are employed for staining bacteria, especially methyl and gentian violet, methylen blue, fuchsin, and Bismarck brown. They are kept in stock solutions (saturated alcoholic) and enough is taken at a time to color a 50 cc. bottle of distilled water so that the neck is just transparent, or added to a watch glass of distilled water to the point when the fluid becomes too dark to see through; in such strengths these dyes will stain nearly all forms of bacteria; the thin solutions are good for about two weeks. To such solutions certain mordants are added to increase the power of the staining agent, and alkalis, carbolic acid, anilin and ammonium carbonate are the commonest. Thus

1. Löffler's Methylen Blue :

Concentrated alcoholic methy-	
len blue,	30.00
0.01 per cent. potassium hy-	
drate solution,	100.00

This stains quickly, 5-10 minutes, and is fairly durable; for organisms hard to stain the potassium may be raised to 1.0 per cent.

2. Anilin gentian violet :

Anilin oil,	10 parts.
Distilled water,	100 "

Shake thoroughly till milky, let stand, filter through moist filter, then add

Concentrated alcoholic solution	
gentian violet,	10 cc.
Alcohol (for preservative),	10 cc.

This gives good results but is not very durable, requiring renewal about every ten days.

3. Carbolic fuchsin mixture :

Fuchsin,	1.00
Alcohol (absolute),	10.00
Mix, then add	
5 per cent. solution carbolic acid,	100.00

This is very satisfactory for many kinds of bacteria, and one of the best for rapid diagnosis of tubercle bacilli, the preparation being gently heated in this stain till steam appears, washed, excess of color removed by acid alcohol, examined in water or dried and mounted.

4. Carbolic methylen blue :

Methylen blue,	1.5
Alcohol (absolute),	10.00
5 per cent. carbolic acid,	100.00

To differentiate, by removing excess of stain, or decolorizing certain forms while others remain colored, the usual fluids are :

Alcohol, 70-90 per cent.

Anilin, with or without xylol added.

Alcoholic solution of acid anilin dyes, fluorescein, tropaeolin, eosin.

Acetic acid (0.5 to 1 per cent.) in water.

Iodine-iodide of potassium solution.

Picric acid in watery or alcoholic solution, usually weak.

Mineral acids in water or alcohol (1-25 per cent.).

The first four act gently and leave nuclei and bacteria colored, removing the stain from fibrin, mucus, cell plasma and basement substance ; the others act more strongly.

Cover-glass Preparations.—With a sterile platinum loop a small drop of the material to be examined (for fluids use the centrifuge and take a little of the sediment) is put upon a clean cover-glass and gently spread in a uniform layer ; or two cover-glasses are applied to each other with the material between and

gently slid apart ; dry in air with protection from falling dust, or gently over a Bunsen burner ; if the latter, holding the cover-glass (smeared side up) in a forceps, describe with it a perpendicular circle of about half a meter diameter, a portion of the downward arc passing evenly through the flame, contact lasting about a second, repeat twice ; the best forceps is one which opens only on firm pressure, holding the cover-glass without effort on the part of the user. The heat fixes the albuminous matter and the preparation may be stained without fear of washing it off. The stain is dropped on the smeared side from a pipette and if haste is necessary its action is quickened over the flame ; then dried and mounted in xylol balsam. Or with a little practice, the cover-glass may be floated on the surface of a staining solution and left there several hours. Löffler's blue is allowed to act in the former case 0.5 to 2 minutes, methylen-blue 3 to 5 minutes ; after gentian violet and fuchsin, wash in acetic acid water (1 to 300), then in water, dry in air, mount. Preparations with methylen-blue may be decolorized in equal parts of water and concentrated solution of carbonate of potassium, only the bacteria retaining the stain ; after washing, a different stain, as Bismarck brown, may be used for the tissue elements.

5. Gram's Method.

Cover-glass fixed and stained in gentian violet 3 to 5 minutes.

Put for 1 to 2 minutes in—

Iodine,	1.0
Potassium iodide,	2.0
Water,	100.0

Decolorize in alcohol till grayish-yellow, dry and mount : for double staining, after the alcohol use Bismarck brown, wash in alcohol, mount. Acid added to the alcohol hastens its action and prevents precipitation ; 3 per cent. HCl or 10 to 20 per cent. acetic. The preparation

coming out of iodine solution into pure alcohol, then into the acid alcohol, again into pure alcohol, and double stained as before, though Bismarck brown does not do so well.

This method stains nuclei, bacteria (with exceptions), horny epithelium, mast cell granulations. For a second stain the following is recommended :

6.

Fuchsin,	1.0
Carbolic acid, glacial,	5.0

Rub together till the acid is dissolved, add while steadily rubbing.

Glycerin,	50.0
Distilled water,	100.0

To use, dilute with water to a tenth, stain 1 minute, with gentle heat, wash carefully in water.

The following bacteria are

Stained by Gram's Method.

Anthrax bacillus,
Tetanus bacillus,
Diphtheria bacillus,
Leprosy bacillus,
Tubercle bacillus,
Rhinoscleroma bacillus,
Diplococcus of pneumonia,
Streptococcus pyogenes,
Streptococcus erysipelatis,
Staphylococcus pyogenes (all forms),
Micrococcus tetragenus,
Oidium albicans,
Actinomycosis,
Many saprophytes.

Not Stained by Gram's.

Typhoid fever bacillus,
Malignant edema bacillus,
Plague bacillus,
Coli communis bacillus,
Pyocyaneus bacillus,
Glanders bacillus,
Influenza bacillus,
Cholera asiatica spirillum,
Relapsing fever spirochete,
Gonorrheal diplococcus,
Bacillus of pneumonia
(Friedländer's).

To Stain Spores.—1. Müller's method.

Cover-glass preparation, dry in air, fix in flame.

Float 5 seconds to 10 minutes on 5 per cent. chromic acid in water; each kind must be tested, anthrax and tetanus require 2 minutes.

Wash in water.

Stain with anilin fuchsin or carbolic fuchsin 1 minute with heat.

Decolorize 5 seconds in 5 per cent. sulphuric acid.

Wash in water.

Stain in aqueous methylen-blue 3 minutes.

Wash in water, dry, mount.

2. Make cover-glass preparation, float on it a layer of Löffler's alkaline methylen-blue, hold over a gas flame and boil, remove for a few minutes and then heat again, wash in water, dip in 95 per cent. alcohol with 0.3 per cent. hydrochloric acid five or six times, wash in water, stain 8–10 seconds in anilin water fuchsin; if successful the spores are blue and the other elements red.

3. Or the cover-glass may be floated on the surface of carbolic fuchsin in a watch glass, this heated to boiling over flame and cooled a little, again heated and cooled a few times; allowed to stand five minutes; placed without washing and charged side up in 3 per cent. hydrochloric acid alcohol and tilted back and forth one minute, double stained with methylen-blue; the spores are red and the other elements blue.

To Stain Flagella. *Bunge's Method.*—Prepare a saturated solution of tannin and a solution of 1–20 liq. ferri sesqui-chlor. in distilled water; to 3 parts tannin add 1 part iron solution; to 10 cc. of this add 1 cc. concentrated watery fuchsin solution—the mordant should be exposed to the air two or three weeks before using. After preparing a cover-glass with a dilute drop of culture, drying in air and fixing in the flame, the mordant is used cold for five minutes and then gently heated a long way above a gas flame; wash in water, dry, stain slightly with

carbolic fuchsin and examine. Other methods are more complicated; see Löffler's and Van Ermengem's in standard textbooks.

To Stain Capsules.—Prepare cover-glass, float a layer of glacial acetic acid on it and at once pour it off, drop on gentian violet anilin-water solution and pour off, another dash of stain, again poured off; wash in sodium chloride solution 0.7-1.5 or 2 per cent. (the right strength can be told only after experiment).

For staining sections of tissue to show bacteria, very small and thin pieces must be hardened in sublimate, formalin, or absolute alcohol; imbedded in paraffin; the sections stained by one of the dyes or mixtures given, but for twice or three times as long, perhaps with the assistance of heat (27-40° C.). To differentiate, water with or without acid, anilin and alcohol are used, and also Gram's method; dehydrate in absolute alcohol, clear in xylol, mount in xylol balsam. Counter-staining is often desirable.

CHAPTER XII.

TABLES AND STATISTICS.

The Metric System.

METER.	GRAM.	LITER.
10,000 = myriameter		10,000 = myrialiter
1,000 = kilometer		1,000 = kiloliter
100 = hektometer	10,000 = myriagram	100 = hektoliter
10 = dekameter	1,000 = kilogram ² =	10 = dekaliter
1 = METER	100 = hektogram	1 = LITER
.1 = decimeter	10 = dekagram	.1 = deciliter
.01 = centimeter ¹ =	1 = GRAM	.01 = centiliter
.001 = millimeter	.1 = decigram	.001 = milliliter
	.01 = centigram	
	.001 = milligram	

EQUIVALENT VALUES.

1 meter,	39.37 inches.	1 grain,	0.065 gm.
1 centimeter,	$\frac{1}{2}$ inch (0.4).	1 minim (usually),	0.06 cc.
1 liter,	1.05 quarts, 2.11 pints.	1 drachm,	3.96 gm.
1 gram, or (in most cases)	} 15.43 grs.	1 ounce,	31.68 gm.
1 cubic centimeter,		1 ounce, glycerin,	37.00 gm.
1 milligram,	$\frac{1}{16}$ (0.015) gr.		
1 kilogram, {	2.2 pounds avoirdupois,		
	2.7 pounds troy.		
1 millimeter,	$\frac{1}{32}$ inch (0.039).		

To convert grains into milligrams, multiply by 6479.

¹ One cubic cm. of water at its greatest density, 4° C., weighs 1 gm.

² One kilo of water at its greatest density, 4° C., measures 1 l.

Thermometers.

To change Fahrenheit degrees to Centigrade :

Subtract 32, multiply by 5, divide by 9: thus

Normal human temperature, 98.6° F., equals 37° C., for

$$98.6 - 32 = 66.6 \times 5 = 333.0 \div 9 = 37.$$

To change Centigrade degrees into Fahrenheit :

Multiply by 9, divide by 5, add 32 ; thus

Fever temperature, 40° C., equals 104° F., for

$$40 \times 9 = 360 \div 5 = 72 + 32 = 104.$$

Relative Length of Body Parts.		Actual and Relative Weights.	
The Body taken as 1,000.	The Hand taken as unity.	Actual Kilo.	Hand as unity.
Body, ...1,000	8.50	64.00	118.46
Trunk, ...306.9	2.59	29.63	54.845
Upper extremity, ...501.75	4.26	3.77	6.983
Lower " 570.3	4.85	11.14	20.62
Head and Neck, ...122.7	1.043	4.56	8.44

Example.—If the hand alone should be found, the probable height of the person from whom it came would be 8.5 times the length of the hand from wrist joint to tip of middle finger, and the weight would approach the weight of the hand multiplied by 118.46: should the headless and limbless trunk be studied, the total height would be the excess over the trunk percentage, as above, added to the length of the same, and the weight would be found in a similar way or by rule of three. An upper extremity measuring 29 inches would be 4.26 times the hand; dividing the former by the latter would give the hand as 6.8 inches long; the total height would be 8.5 times this, or 5.78 ft.

These tables, compiled in Germany, are not wholly accurate for the mixed population of the United States.

THE ADULT SKELETON.—AVERAGE TOTAL WEIGHT 9,814 GM.

Length in Cm.	Male.	Female.
Total skeleton.....	162-172	151-162
Sternum.....	18-20	16-17
Clavicle.....	14.2	13.6
Humerus.....	32	30
Ulna.....	26	23
Radius.....	24	22
Hand.....	20	18
Outer lip of iliac crest to opposite.....	28	30
Femur.....	55	43
Patella.....	4	4
Tibia.....	39	34
Fibula.....	37	33
Foot.....	24	22
Angle between neck of femur and shaft.....	127-135°	112-125°

PELVIC DIAMETERS, INLET.

	MALE.	FEMALE.
Conjugate,	10.8	11.6
Oblique,	12.2	12.9
Transverse,	12.8	13.5
Circumference,	40.6	44.7

NEW-BORN CHILD'S HEAD, DIAMETERS.

Fronto-occipital,	11.75
Biparietal,	9.25
Bitemporal,	8.00
Mento-occipital,	12.5
Circumference,	34.5

THE AVERAGE ADULT ORGANS.

Organ.	Weight in Gm.		Proportion to total Weight (assumed as 66.2 K., male, 25 yrs.).	Proportion to the New-born as Unity.
	Male.	Female.		
Brain.....	1,430	1,224	2.16	3.76
Lung, R.....	512	458	0.77	16.97
" L.....	482	416	0.73	20.14
Heart.....	300	260	0.46	12.74
Liver.....	1,819	1,664	2.75	12.84
Kidneys.....	305	291	0.46	13.12
Spleen.....	163	173	0.25	15.38
Stomach.....	183			
Small intestine.	718			
Large "	174			
Pancreas.....	89.7		Total weight,	21.36

Specific gravity of normal adult cadaver 0.9213.

DIMENSIONS OF CERTAIN ORGANS IN MM.

Organ.	New-born.		Adult.	
	Length.	Breadth.	Length.	Breadth.
Liver	115	88	320	190-210
Gall-bladder ..	32		80-110	34
Pancreas.....	54	20	190-220	40
Spleen....	40	18	120	75
Thymus	54-83	27-41		
Kidney	45	27	108-114	54-63
Ureter.....			320-340	

LENGTH OF ALIMENTARY CANAL IN CM.

	New-born.	Adult.
Incisor teeth to cricoid cartilage	7	14.8
Incisor teeth to cardiac opening	17	40
Stomach	4-5	27-32
Small intestine	260-350	5,650
Large intestine.....	42-48	160

CAPACITY IN CC. OF

Stomach, during life,	1,600-1,700
post mortem,	2,900
Small intestine,	6,200
Colon,	4,850
Urinary bladder, up to	400
Gall-bladder,	33-35
Corresponding to	
Bile, in grams,	33.5-37
Skull: adult male, 1,500; female, 1,300.	

DIMENSIONS OF THE UTERUS.

	Virgin.	End of Pregnancy.
Length	74-81 mm.	320 mm.
Breadth	34-45	270
Capacity	3.5-5.0 cc.	4,960-5,000 cc.
Weight	33-41 gm.	700 gm.

Placenta, average weight 500-790 gm.; usually 75 gm. heavier with boys than with girls.

Total bodily surface, about 1.75 square meters. Pressure of atmosphere upon this surface :

At sea level,	18,000 Kilo.
1,000 feet or 303.6 meters above sea level,	15,860
At 5,000 feet,	9,600

THE HEART—About the Size of the Individual's Fist.

Dimensions in cm.	Empty.	Slightly Distended.	At Birth.
Length	12.9	14.9	9
Breadth	9.5	10.8	10.7
Thickness	6.8	8.8	3.6
	Male.	Female.	
Weight in gm.....	340-375	285-300	20.6
Proport'n to total..	1:169	1:149	

DIAMETERS OF CARDIAC ORIFICES IN CM.

	Male.	Female.
Aortic.....	1.0	0.9
Mitral.....	1.4	1.2
Pulmonary.....	1.2	1.1
Tricuspid.....	1.8	1.5

The taller the individual the heavier the heart, and the larger the diameters of valve openings.

GREATEST THICKNESS OF WALLS OF CHAMBERS IN CM.

	Male.	Female.
Right Auricle.....	0.2	
Left Auricle	0.3	
Right Ventricle.....	0.6	0.4
Left Ventricle.....	1.7	1.6
Septum, Ventricular.....	0.9-1.2	
Septum, Auricular.....	0.25	

	Male.	Female.	New-born.
Total capacity,	320-380 cc.	256-320 cc.	20.6

CIRCUMFERENCE OF MAIN VESSELS IN MM.

	Adult.	At Birth.
Ascending Aorta	70-76	18-20
Pulmonary.....	65	23.5
Abdominal bifurcation ...	32	

Daily work of heart, 20,000 kilogram-meters : the kgm. equals one kilo lifted one meter, or 2.2 pounds a little over a yard and three inches.

Total blood in adult 4 5-5 kilo, equals about $\frac{1}{13}$ body weight.

Average blood-pressure in large vessels.

New-born,	111 mm. of mercury.
At 14 years,	171
Adult,	200

Time of circulation (adult weighing 63 kilo, pulse beat 72) 22 seconds, or about while the heart beats 26-28 times.

DIMENSIONS OF RED BLOOD CELL.

Average greatest diameter,	7.74 μ
Thickness of edge,	1.9
Thickness of middle,	0.99
Superficies,	128 sq. μ

BLOOD CELLS IN CUBIC MM.

Adult.	Male	Female.
Red Cells.....	5,221,000	4,886,000
White Cells.....	6,000	6,500
Proportion of Red to White.....	1:830	1:750

	Adult.	New-born.
Average time required for coagulation,	9.28 min.	18.0 min.

NERVOUS SYSTEM.

	Male.	Female.
Brain, average weight in gm....	1358	1,235
specific gravity.....	1.0386	
breadth of convolutions		
in mm.....	5-17	
depth of fissures.....	12-23	
thickness of cortex.....	2.94-2.91	
Cord, average length in cm...	44 8	41.7
average weight in gm.	39.15	
number of spinal nerves	31 (rarely 32)	
depth of anterior fissure		
in mm.....	2-4	
depth of posterior fissure in mm.....	4-6	
Length of spinal column in cm.	69-70	66-69
about $\frac{2}{3}$ the height.		

TABLE OF ANTISEPTIC SOLUTIONS WHICH INHIBIT THE GROWTH OF BACTERIA.

Alum,	1 part to	222 water.
Aluminum acetate,	6,000	"
Ammonium chloride,	9	"
Boric acid,	143	"
Calcium chloride,	25	"
Calcium hypochlorite,	1,000	"
Carbolic acid,	333	"
Chloral hydrate,	107	"
Copper sulphate,	2,000	"
Iron sulphate,	200	"
Formaldehyde, pure,	25,000	"
Formaldehyde, 40% sol.	10,000	"
Hydrogen peroxide,	20,000	"
Mercuric chloride,	14,000	"
Mercuric iodide,	40,000	"
Potassium bromide,	10	"
Potassium iodide,	10	"
Potassium permanganate,	300	"
Quinine sulphate,	800	"
Silver nitrate,	12,500	"
Sodium borate,	14	"
Sodium chloride,	6	"
Zinc chloride,	500	"
Zinc sulphate,	20	"

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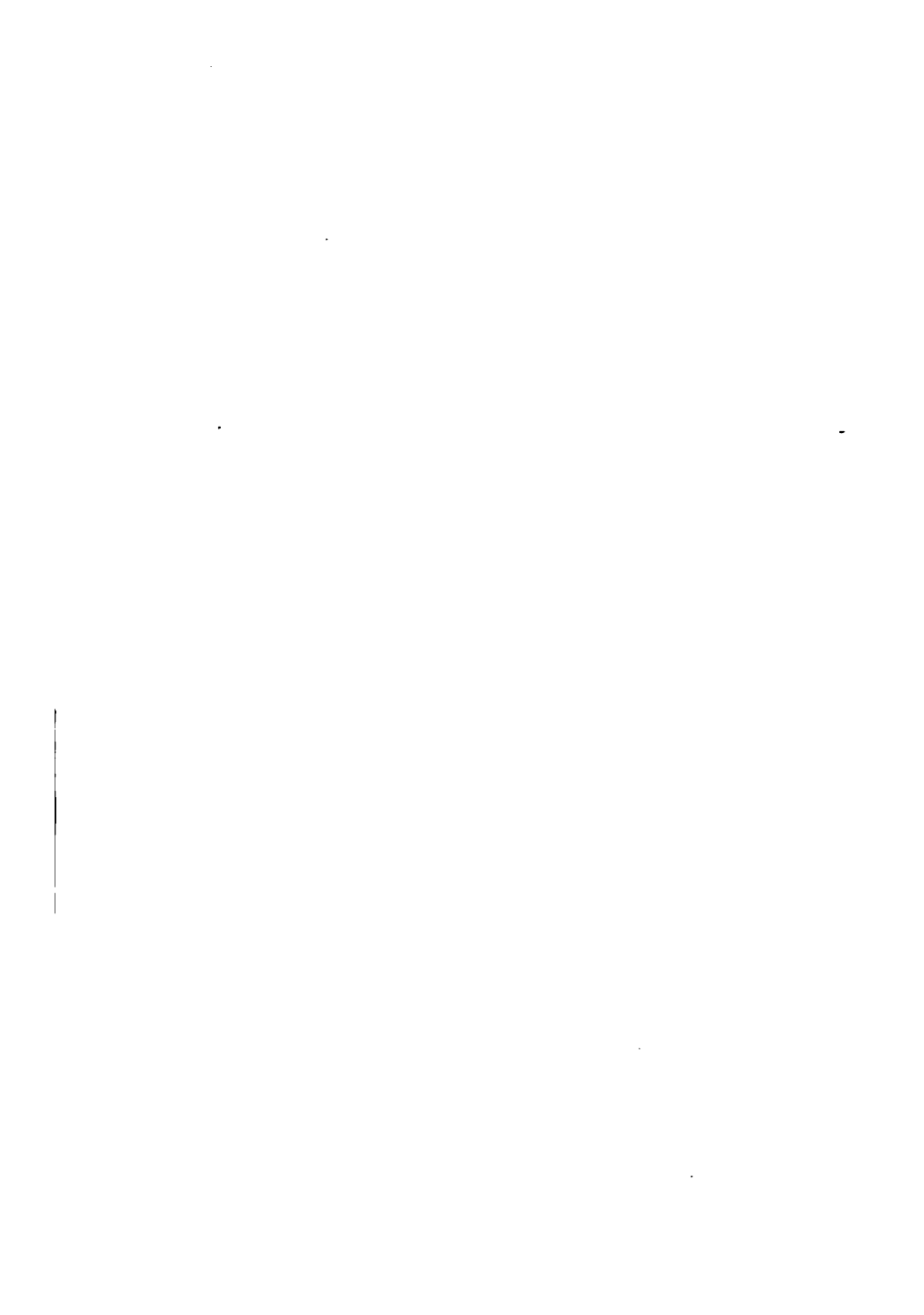
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